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THE JOURNAL

SOUTH CAROLINA MEDICAL ASSOCIATION

SOUTHERN SOCIETY OF ANATOMISTS
MINUTES OF COUNCIL

VOLUME 71

JANUARY 1975

NUMBER 1

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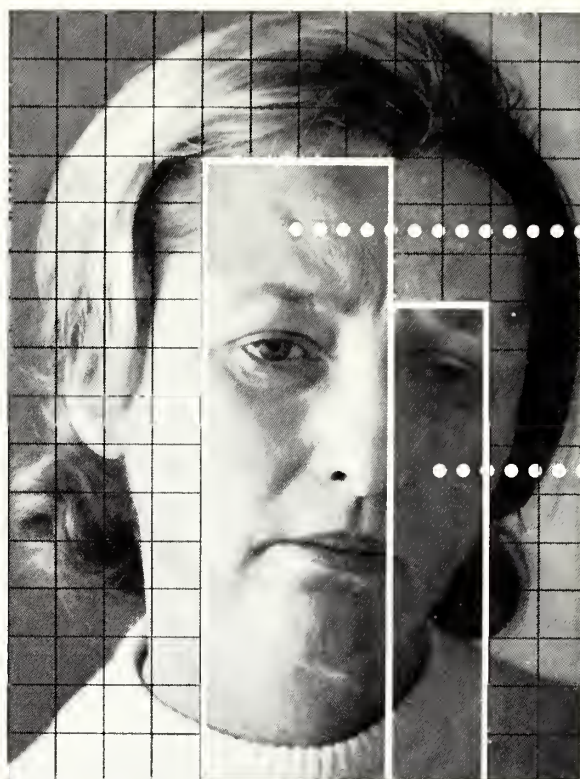
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anxiety

Associated
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symptoms

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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

JUN 12 1975

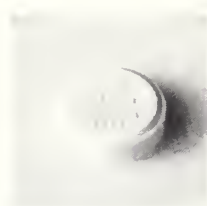
respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

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in psychoneurotic
anxiety states
with associated
depressive symptoms

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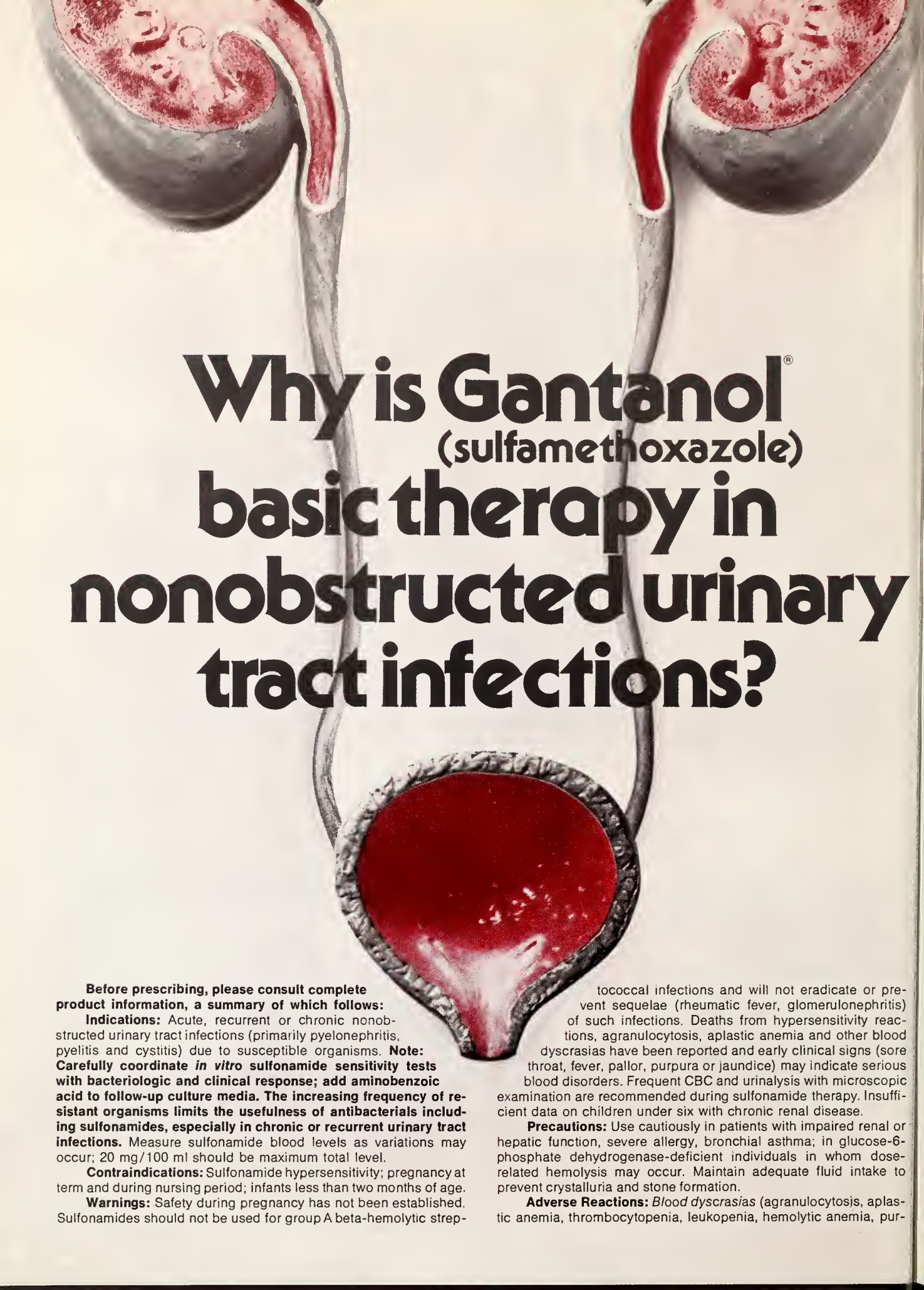
Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic strep-

tococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

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pura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

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Length—Short articles of about 2,500 words (about 8 typewritten pages, double spaced) are preferred. Longer articles will defer to the shorter ones in schedule of publication.

Manuscripts should be typewritten, double spaced, and the original and a carbon copy submitted.

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Complete literature available on request from Professional Services Dept. PML.



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THE JOURNAL

SOUTH CAROLINA MEDICAL ASSOCIATION

VOLUME 71

JANUARY, 1975

NUMBER 1

SOUTHERN SOCIETY OF ANATOMISTS

14th ANNUAL MEETING

The Southern Society of Anatomists 14th Annual Meeting was held from October 10 to 12, 1974, at West Virginia University, Morgantown, West Virginia. Official abstracts of the meeting follow.

BENSON, M.; CARMICHAEL, S. W.; GARDNER, L. W. and BROWN, C., Department of Anatomy, West Virginia University, Morgantown, West Virginia.

The fine structure of the adrenal medulla of lesser bushbaby (*Galago senegalensis*) and tree shrew (*Tupaia glis*) was studied after immersion fixation in 3% glutaraldehyde. Only one cell type was observed.

The most prominent observation was the distribution of chromaffin vesicles, of which there were two types. The more numerous vesicles were dark and dense; the other vesicles were usually larger and less osmiophilic. Both types of granules were membrane bound, often containing a space of light electron density between the vesicle contents and surrounding membrane. Bushbaby and tree shrew differed in the clustering arrangement of the vesicles.

Long and slender nerve processes were in complex association with the cells. Both dense-cored and light-cored vesicles were seen in nerve cross-sections. Other clear cored vesicles were scattered throughout the cytoplasm.

Collagen fibers were components of the stroma and blood vessels with fenestrations of the endothelial wall were observed. Plasma membranes occasionally interdigitated at cell boundaries.

Differences in location of mitochondria were apparent in the two animals studied. Both bushbaby and tree shrew contained rough endoplasmic reticulum and polyribosomes.

The nature of the dark and light vesicles is discussed.

BERESFORD, W. A., Department of Anatomy, West Virginia University, Morgantown, West Virginia. *The development of the penile bone of the rat.*

Paraffin sections were stained with H. & E. or Lison's method (Stain Technol. 29, 131). Whole penises were treated with KOH-Alizarin red.

The genital tubercle of the newborn male rat has an elongated densely cellular region just dorsal to the urethra and distal to the forming corpus fibrosum. One day postnatally the cells start depositing a non-trabecular bone (distinguished from osteoid by staining with alizarin red). At two to three days alcian-blue-positive cartilage forms proximally and attached to the bone, thus being a true secondary cartilage. At four days, osteoclasts erode into the shaft adjacent to the cartilage which then becomes an endochondral growth cartilage closely resembling the mandibular condyle. Part of the resem-

blance lies in the layering, presence of chondroclast cells, and apparent absence of dead hypertrophic chondrocytes. The bony shaft undergoes minor internal remodelling while its thickness increases by slow periosteal deposition. The distal tip is large-celled or chondroid bone. The cartilaginous base is separated from the compact shaft by a trabecular region which remodels to become the proximal shaft and a marrow-filled basal bulb. Finally, the growth cartilage is consumed except for a small dorsal spur of fibrocartilage. This relatively simple and isolated bone, forming after birth, may provide a model useful for studying the role of hormonal, mechanical, electrical and other factors in influencing the growth and regression of bone and cartilage. Valid and worthwhile comparisons may be drawn with developmental processes in such bones as the mandible and antler.

BRESNAHAN, J. C. and MARTIN, G. F., The Ohio State University, Columbus, Ohio. *A neuroanatomical analysis of spinal cord injury in the rhesus monkey (Macaca mulatta)*.

Nine rhesus monkeys were subjected to impacts of either 200, 300, 400 or 500 gr-cm of force on the dorsal surface of the upper thoracic spinal cord (Allen, 1911). Four additional control animals were subjected to either cord transection at the same level or the operative procedure alone. One week after surgery, the animals were sacrificed and the brains and spinal cords were processed by the Fink and Heimer (1967) technique for degenerating axons.

After cord transection, axonal degeneration was observed in all of the ascending, descending, and local systems previously described in the literature. The location of degeneration following all impacts was identical to that present after transection, but there were variations in quantity from animal to animal. However, such variations were not directly proportional to the impact force.

The portion of the spinal cord above

the central canal was found to be particularly susceptible to hemorrhagic necrosis. These data, in conjunction with previous findings, suggest that the resolution of force was concentrated at the base of the dorsal $\frac{1}{2}$ of the cord regardless of the level at which the damage occurred. Whether this is a function of poor blood supply to this area, or the structural properties of the cord, or a combination of these and other factors, remains to be elucidated. (Supported by HEW, PHS, NIH — Neurol. Diseases and Stroke Contract #5P01 NS10165-03.)

BROWN, P. B., Dept. of Physiology & Biophysics, West Virginia University Medical School, Morgantown, West Virginia. (Introduced by J. Culberson). *Somatotopic organization of hindlimb skin area of cat dorsal horn*.

Single-unit recordings were obtained from low spinal cats. The dorsal horn representation of the hindlimb was examined in segments L₃-S₂, primarily in laminae IV-VI. The antero-posterior distribution of receptive fields was organized such that each dorsal horn dermatome was most similar to its corresponding dorsal root dermatome. The mediolateral dorsal horn gradient can equally well be described as distoproximal on the limb or embryologically ventrodorsal.

There was no effect of laminar location on receptive field location. Laminar location was also unrelated to receptive field size or shape, central delay, or spontaneous discharge.

The results are consistent with the known anatomy of the dorsal horn. In conjunction with earlier electrophysiological results, they suggest that (a) the presynaptic neuropil of substantia gelatinosa is somatotopically organized; (b) the apparent wide divergence of dorsal root terminations represents a fiber-sorting mechanism; (c) the cutaneous receptive fields of deeper cells are largely determined by the portion of the gelatinosal neuropil penetrated by their dorsal dendrites.

BUTCHER, R. L., Department of Obstetrics & Gynecology and Department of Anatomy, West Virginia University, Morgantown, West Virginia. *Alterations of steroids and gonadotropins in the rat during delayed ovulation as a cause of abnormal embryonic development.*

The frequency of birth defects is increased in the offspring of women under 15 and over 40 years of age. These are times when the hormonal balance is undergoing change and the menstrual cycles are often irregular. It was proposed that hormonal imbalance results in delayed ovulation with detrimental effects on the preovulatory oocyte. Previous work from this laboratory has shown that an induced or spontaneous delay of ovulation for 48 hours in the rat results in both morphological and chromosomal abnormalities. The present study was carried out to determine if a delay of ovulation produces changes in hormonal concentrations in plasma which could be responsible for alterations in the oocyte.

Rats were killed by decapitation at 3-hour intervals during a 48-hour delay of ovulation induced by sodium pentobarbital, as well as during the ensuing delayed proestrus, estrus and the first 4 days of gestation. Control animals were killed at identical times following injections of vehicle. Blood was collected and analyzed for LH, FSH, prolactin, progesterone and estradiol-17 beta to determine if alterations in hormonal levels occurred, which could account for abnormal embryonic development following delayed ovulation. Hormonal concentrations in plasma were measured by radioimmunoassay except for progesterone, which was determined by competitive protein binding. Embryos were examined to verify the occurrence of abnormal development in the present study. Rate of oocyte maturation was studied in serial sections of ovaries from all animals killed at 30-minute intervals on the afternoon of proestrus.

Oocytes remained in meiotic arrest during the 48-hour delay of ovulation, but

resumed maturation at the expected time on the afternoon of the preovulatory surge of gonadotropins. Abnormal embryonic development was significantly increased following delayed ovulation. A number of alterations in hormonal levels during the preovulatory period are discussed as possible mediators of abnormal embryonic development. Patterns of estradiol concentration in plasma were changed markedly, and appear as the most likely of the hormones studied to alter both the oocyte and the intrauterine environment. Hormonal concentrations in plasma during the preimplantation period were not altered by delayed ovulation.

CARMICHAEL, S. W.; SMITH, D. J. and WILLIAMS, T. W., Departments of Anatomy and Anesthesiology and Pharmacology, West Virginia University, Morgantown, West Virginia. *High-voltage electron microscopy of the adrenal medulla: a three dimensional slide presentation.*

Cats and rats were used for this study. The adrenals were perfused with either a dilute Karnovsky's fixative or 3% glutaraldehyde. The medulla was post-fixed in 2% osmium tetroxide or 3% potassium permanganate. The tissue was dehydrated in ethanol, embedded in Epon, and sectioned at 0.5 micron with glass knives. Sections were stained up to an hour each with uranyl acetate and lead citrate. Electron micrographic stereo pairs were taken at 10,500X with a 24 degree tilt angle using the one million volt EM at United States Steel Research Laboratory in Monroeville, Pennsylvania. Enlargements were made (3X), photographed with color positive transparency film, and mounted for stereo projection. The slide is projected with a stereo projector onto a polarized screen and the audience, wearing polarized glasses, receives a three-dimensional view of the ultrastructure.

The membranes near the surfaces of the sections were clearly visible. A significant percentage (15%) of catecholamine granules were seen to be tubular in shape, although they have been described as

spherical in these species. This suggests that catecholamine granules are tubular at some stage in their development, and that this is best demonstrated in thick sections. Other morphological aspects of catecholamine granule formation and secretion are being studied by HVEM.

(This work was supported by a W.V.U. Senate Research Grant and N.I.H. Contract 70-4136.)

DAVENPORT, W. D., Jr. and McDONALD, T. F. Department of Anatomy, Medical College of Georgia, Augusta, Georgia. *Capillary development in the thymus as related to the development of the blood-thymus barrier (BTB).*

Examination of the blood-thymus barrier (BTB) in fetal and post-natal thymuses from animals ranging from 15 days gestation to beyond 6 weeks post-partum reveals that after capillary formation occurs, there is still some delay in the maturation of the barrier itself. The BTB is composed of (1) a continuous endothelial lining, lacking fenestrae or any structures resembling weaknesses or pores; (2) a definite and continuous basement membrane (BM) which may be slightly thickened; (3) vessel investment by phagocytic reticular cells (PhRC); and (4) tight junctions or zonula occludentes between endothelial cell processes. By the time the vessel is patent, the BM and PhRC investment is fairly well developed. With respect to these two criteria, there are no striking differences between late fetal and early post-natal specimens. During post-natal development of 10-14 days, what appears to be tight junctions can be seen. In thin section, what resembles the internal leaflets of such a junction can be distinguished. By post-natal day 15, thickenings or densities on the intracellular surfaces of adjoining cell membranes can be seen. By post-natal days 21-24, these thickenings are found to be as well developed as those found in the vessels of mature animals (6-8 weeks). Taking these intracellular densities as a sign of complete maturity, and assuming

that these thickenings do, in fact, have some functional relevance to the BTB, it can be stated that the BTB shows no sign of functional maturity until post-natal day 15 and beyond. This could have some bearing on the development of the cell mediated immunity (CMI) system in the mouse which is not fully developed until after post-natal day 15.

DeNEE, P. B., Ph.D., Appalachian Laboratory for Occupational Respiratory Diseases, National Institute for Occupational Safety and Health, Morgantown, West Virginia 26505. *Biomedical applications of backscattered electron imaging: one year's experience with sem histochemistry.*

We have investigated the usefulness of backscattered electron (BSE) imaging in the scanning electron microscopic (SEM) study of biological samples. Direct correlation of surface morphology, as revealed in the secondary electron (SE) mode, with familiar histopathology is achieved using atomic number contrast in the BSE mode. An image resembling a light microscope (LM) or transmission electron microscope (TEM) image is obtained with the BSE mode using reversed signal polarity. The resolution of the BSE mode (250-500A) exceeds that of the LM by 5 to 10 fold. The depth of field of the SEM has even greater advantage of the LM. Owing to greater penetration than the SE, the BSE image reveals stained features several micrometers beneath the specimen surface.

Both naturally occurring variations in atomic number and those produced by specific heavy metal staining of the sample are useful. The BSE mode reveals vascular patterns not seen in the SE mode in unstained lungs in pneumoconioses, as well as the location of retained dust particles. We have developed modifications of existing stains for tissue sections and blocks. Nuclei, nucleoli, reticulin fibers, basement membranes, lysosomes and enzyme activities are readily identified. Treatment of tissues with histochemical reagents after appropriate fixation, fol-

lowed by critical point drying produces no detectable alteration in the fine structural surface morphology as revealed by SE imaging.

We have found the following to be essential for the use of this technique: 1) a solid state backscattered electron detector, located near the pole piece of the final lens; 2) material of low atomic number for coating and support of the sample; and 3) sufficiently high concentration of the staining element (varying inversely with atomic number).

In conclusion, based on one year's initial experience we expect backscatter electron imaging to become at least as valuable in scanning electron microscopy as fluorescence and polarizing microscopy are for light microscopy.

DESESSO, J. M. and JORDAN, R. L., Department of Anatomy, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia. *A comparative study of the teratogenic effects of three drugs on rabbit limb development: Preliminary findings.*

Pregnant New Zealand White rabbits were administered either methotrexate (folate antagonist) or hydroxyurea (DNA synthesis inhibitor) or acetazolamide (carbonic anhydrase inhibitor) on gestational days 12 and/or 13. Teratologic effects of the drugs on near-term fetuses were studied preceding initiation of mechanistic studies of limb dysplasias.

Methotrexate produced cleft palate, micrognathia, fore and hind limb syndactyly, ectrodactyly and adactyly. Combinations and permutations of these lesions affected all fetuses. Histologically, edema and cell death in mesenchymal tissues and hepatic hypertrophy characterized the methotrexate lesions. The apical ectodermal ridges of limb buds from treated embryos appeared smaller and structurally less complicated than those of controls.

Hydroxyurea affected all fetuses with severe skull anomalies, micrognathia, cleft lip and palate, fore and hind limb hemi-

melia, adactyly, ectrodactyly and syndactyly. Inspection of cleared specimens disclosed wavy and fused ribs, scrambled vertebrae as well as osseous defects consistent with the gross anomalies.

Acetazolamide produced retarded fetuses which otherwise exhibited normal gross morphology. Analysis of cleared specimens revealed bilateral aplasia/retarded ossification of the first metacarpal and talus. First metacarpal aplasia is a pre-axial reduction defect; this finding is at variance with previously reported acetazolamide-induced post-axial reduction defects in rat, hamster and mouse.

DOLLAR, J. R.; HAND, G. S.; BECK, L. R.; BOOTS, L. R., Departments of Anatomy and Obstetrics and Gynecology, University of Alabama in Birmingham, Birmingham, Alabama. *Histochemical comparison of proliferative and secretory endometrium of the baboon.*

It is imperative to obtain precise morphological data on the baboon menstrual cycle if this animal is to be used as a model for the study of human reproductive biology. Fifteen adult female baboons having regular ovulatory cycles are available for such a research project. To date our histological and histochemical studies on baboon endometrium have been limited to the proliferative and secretory stages with research planned for studying at least five different stages on all fifteen animals. Staging of the ovarian cycle is determined by blum turgescence which is correlated with hormone assays of blood samples.

Endometrial tissue obtained by curette biopsy was prepared for routine light and electron microscopy and for histochemical studies. Cryostat sections of quickly frozen endometrium were studied for alkaline and acid phosphatase activity by both Gomori's lead salt technique and by Pearse's azo dye method. Glycogen content has been studied with the PAS technique in conjunction with diastase digestion. Additionally, other histochemical studies are in progress.

Alkaline phosphatase, located in the apical half of the endometrial gland cells, demonstrates strong activity during the late proliferative stage. During the secretory period the activity of this enzyme diminishes markedly. In contrast, acid phosphatase demonstrates little activity within the glands at ovulation, but within six days, acid phosphatase activity has increased significantly. The staining reactions also demonstrate this activity within the apical half of the glandular cells. At ovulation the apices of endometrial gland cells contain considerable amounts of PAS-positive material which is not sensitive to diastase digestion. However, within the secretory phase endometrium all granular-appearing PAS-positive material is removed following diastase treatment indicating that glycogen comprises the bulk of the PAS-positive material of this stage. Additional studies are planned to characterize the diastase-resistant carbohydrate. Supported by RF Grant — 70097.

FALLS, W. M. and KING, J. S., Department of Anatomy, The Ohio State University, Columbus, Ohio. *The facial motor nucleus of the opossum: A correlated light and electron microscopic study.*

The normal cytology and synaptology within the facial motor nucleus of the American opossum was studied by use of Nissl preparations, Golgi impregnations, 1 micron plastic sections and electron microscopy. Three categories of neurons are apparent in all regions of the nucleus and are differentiated by their size, Nissl pattern and dendritic arbors. The perikarya of large nerve cells are 30-50 micron in their greatest dimension, exhibit large Nissl granules and display dendrites that span more than one-half the nucleus in the transverse plane. Their proximal dendrites measure 4-7 micron in diameter, taper to 0.5-1 micron and display few spines. Medium neurons are distinguished by their size (20-30 micron), the more rounded shape of their cell bodies and a less extensive dendritic expanse. Their

proximal dendrites are 4-5 micron in diameter, taper to 0.5-1 micron and are relatively aspiny. The smallest neurons (10-20 micron) exhibit a thin rim of cytoplasm which appear either achromatic or uniformly basophilic. Their dendrites are fine, relatively unbranched and generally number two or three.

The cross-sectional diameters of dendrites measured in electron micrographs form the basis for determining the distribution of different populations of synaptic profiles on proximal (4-7 micron), intermediate (2-4 micron) and distal (0.5-2 micron) dendrites. Large and medium neurons are the most numerous and thus contribute the majority of dendritic profiles seen in electron micrographs. A tentative classification of synaptic terminals is proposed based on vesicle shape: (1) spherical, (2) pleomorphic, or (3) ellipsoidal. The size and packing density of vesicles and the size and shape of the synaptic profiles suggest further subdivisions. The different character of terminal degeneration seen after interruption of multiple afferents to the facial motor nucleus (Dom, Falls and Martin, 1973, J.C.N., 152:373) may be reflected in the various types of synaptic endings present and thus provide a good model for the study of connectivity in a lower motor neuron pool.

FREDERICKSON, R. G. and CONE, T. M., Department of Anatomy, West Virginia University, Morgantown, West Virginia. *The subdural space in the guinea pig.*

Precise anatomic descriptions of the membranous coverings of the brain are difficult to obtain because of the fragile nature of cells and extracellular materials comprising the leptomeninges. This is especially true since the dura forms a tough barrier. This study was undertaken in order to devise a suitable method for obtaining brain tissue with properly attached meninges and to demonstrate the fine structural characteristics of the subdural space. Guinea pigs were perfused

with Karnovsky's fixer and the subdural space was examined by electron microscopy. Various regions were observed, including areas near the falx and tentorium. Initially the dura and arachnoid were examined separately after "peeling" the one from the other. Later the tissues were examined together after removal by a special technique. A high speed Mototool with attached miniature circular saw blade was used to cut through bone, dura, arachnoid, pia and brain tissue in selected areas to produce single wedge-shaped samples.

The region between arachnoid and dura is not empty space or merely a fluid-filled potential space akin to the pleural cavity. It contains extremely flattened cells organized in layers of attenuated sheets. In regions over lateral aspects of the hemispheres the subdural cells are organized in only one to three layers. The number of layers increases toward the falx and tentorium until fifty or more layers are found. In fine structure the cells contain very few organelles. The cytoplasm looks quite "hydrated" due to the relative lack of mitochondria, rough endoplasmic reticulum, and general background densities. The cell layers are packed together tightly with only occasional accumulations of rather dense extracellular material in the form of small lakes. Arachnoid cells are firmly attached to the cell membranes of adjacent subdural cells and often there are pools of extremely dense extracellular material in these intercellular spaces. Adjacent cell layers in the subdura are also firmly attached to one another. In fact, when the dura is peeled off the arachnoid, separation occurs as fractures through the cytoplasm of subdural cells, rather than disconnections between opposed cell membranes.

GALLIMORE, L. B., JR., Bowman Gray School of Medicine, Winston-Salem, North Carolina. *Parathyroid hormone, cyclic AMP and the renal retention of calcium in the hamster.*

It is well established that parathyroid hormone plays an important role in the maintenance of serum calcium levels. The early effects of parathyroidectomy (PTX) on urinary excretion and serum concentration of calcium were investigated in young male hamsters, in order to determine how rapidly renal changes, and subsequent changes in serum calcium, could be detected following an abrupt inhibition of parathyroid hormone (PTH) secretion. A significant increase in urinary excretion of calcium would be detected within 15 min. and by 30 min. changes in both urinary excretion and serum concentration of calcium were significantly different from parathyroid-intact controls. Inversely related changes between these parameters continued throughout a 7 h period. Changes in both serum and urinary calcium could be inhibited by intravenous injection of parathyroid extract (PTE), the duration of which was dose-dependent. The percentage of ultrafiltrable and protein-bound calcium fractions of total serum calcium, as well as the clearance of endogenous creatinine were found not to differ significantly between parathyroid-intact and PTX hamsters. From these data it was determined that PTX resulted in a decrease of approximately 30% in the percentage of calcium resorbed from the filtered load. This change was complete as early as 30 min. after PTX. These findings indicate that in the hamster the interaction of PTH and the renal tubules can effect changes in serum calcium of appropriate rapidity and magnitude to play an important role in the minute-to-minute regulation of extracellular fluid calcium. Studies currently in progress suggest that adenosine 3'5' cyclic monophosphate (cAMP) may be involved in this PTH-mediated control of renal calcium retention. Following placement of hamsters on a calcium-deficient diet, changes in amounts of cAMP in both kidney tissue and urine were inversely related to changes induced in the urinary excretion of calcium.

HAZLETT, L. D., Department of Anatomy, Wayne State University, Detroit, Michigan. *Landolt's club in avian retina: A fine structural study.*

The process, first noted by Landolt (1871) in newt and frog retinae has been revealed by Golgi impregnation techniques in numerous species of animals. Survey of the literature, however, reveals a minimum of correlative fine structural data describing the process in the bird. In our Golgi impregnated preparations, the process is seen to arise either as a direct continuation of the dendritic trunk of a bipolar cell or, in some cases, from a branch of the dendritic tuft. It courses through the outer plexiform layer, ending at the level of the external limiting membrane in a terminal expansion approximately 1.0-2.0 micron in diameter. In several instances, a thin cilium-like structure arises from this expansion and extends (2-6 micron) toward the pigment epithelium. Ultrastructurally, the terminal expansion narrows to a slender neckpiece (0.25-0.5 micron in diameter) which in turn expands into a bulbous swelling external to the external limiting membrane. Centrioles are observed within the terminal expansion (9+0 arrangement of microtubules) and in the bulbous swelling, but no cilia are seen. Additionally, the electron microscope reveals the following contacts: club-club, club-photoreceptor cell and club Muller cell. Membrane thickenings are seen in the club-photoreceptor cell contacts, but synaptic vesicles are absent. (This work was supported by Research Grant #477 from the National Eye Institute, National Institute of Health, U.S.P.H.S.)

HENKEL, C. K. and MARTIN, G. F., Department of Anatomy, The Ohio State University, Columbus, Ohio. *The vestibular complex of the american opossum, didelphis marsupialis virginiana.*

The vestibular complex of the American opossum has been studied and compared with that of the cat as described by Brodal and Pompeiano (1957). On the

basis of cytoarchitecture and degeneration experiments which show the distribution of fibers from several extrinsic sources, the four main vestibular nuclei have been identified as well as subgroups 'f,' parasolitaris and 'x.' The superior nucleus contains small (16-25u) and medium-sized (26-39u) neurons which are scattered among cerebellofugal fibers laterally, but more compactly arranged medially. Its larger cells are aggregated centrally. Primary vestibular fibers end within the center of the nucleus whereas fastigial and spinal axons end more peripherally. The lateral nucleus is distinguished by the presence of large (40-60u) neurons. Primary vestibular and crossed fastigial fibers distribute to its ventral region, whereas its extensive inputs from the cerebellar cortex and the homolateral fastigial nucleus tend to end more dorsally. The medial and inferior nuclei are populated by small, medium and large neurons. The medial nucleus includes a rostral region of larger cells, a ventricular border of small neurons, and a caudal area of small and medium-sized neurons. It receives separate, but overlapping projections from the vestibular nerve, fastigial nucleus and spinal cord. The inferior nucleus is distinguished best by the numerous fiber bundles which traverse it. Primary vestibular fibers end within central medial portions of the nucleus, whereas fastigial fibers distribute to its dorsal, lateral rim of small cells and to a compact group of neurons apparently comparable to subgroup 'f.' Neuronal aggregates resembling parasolitaris and 'x' have been identified by their fastigial and spinal inputs respectively. (Supported by Grant NS-07410).

JIMMERSON, V. R.; ROSENQUIST, T. H. and WHEELER, E. J., Department of Anatomy, Medical College of Georgia, Augusta, Georgia. *The effects of castration on the parietal layer of bowman's capsule in the male mouse: A morphometric study.*

The renal corpuscle of the normal adult

male mouse exhibits a rather striking feature, *viz.*, the presence of columnar rather than squamous cells in the parietal layer of Bowman's capsule. The presence of these cells has been shown to be a metaplastic response to androgenic stimulation.

Semi-quantitative study has shown an apparent diminution in the number of renal corpuscles showing metaplasia after castration of the male animal. This study attempts to develop a more sensitive index for quantitation of this phenomenon.

Three mature male BALB/c mice were castrated and the kidneys examined, along with the kidneys of three sham-operated control animals, after a period of four weeks. Tissue samples were perfused with, or immersed in, 0.67M cacodylate buffered 2% glutaraldehyde. Only outer cortex was examined light microscopically, and photomicrographs were made of equatorial profiles of 30 renal corpuscles per animal. Measurements were made on each micrograph to determine "circumferential occupancy" of columnar parietal cells as well as other linear, angular and area parameters for control and castrate animals. Variations in real geometric configuration and fixation artefact were accounted for in assessing results.

The renal corpuscles of castrate male mice showed a decrease in the "percent circumferential occupancy" (*i.e.*, percentage of parietal layer perimeter occupied by columnar cells) compared with those of the controls.

The general utility of this methodology may have wider applicability in morphometry.

KLEINHENZ, M. J.* and SWARTZ, F. J., Department of Anatomy, University of Louisville, Louisville, Kentucky. *Morphological evidence for the role of intranuclear annulate lamellae in pharyngeal glands of ascaris lumbricoides.*

Ultrastructural studies demonstrate abundant annulate lamellae in giant, highly polyploid nuclei of pharyngeal glands in *Ascaris lumbricoides*. Intra-

nuclear annulate lamellae (IAL) are probably derived from the nuclear envelope as suggested by continuity of the two membrane systems and by their similar ultrastructural appearance. The cisternae of IAL are frequently distended by bodies that are classified as light or dark according to their electron density. Light bodies are also located in the cytoplasm and free in the nucleus suggesting that the bodies are transported between cytoplasm and nucleus by annulate lamellae. Dark bodies are found in the cisternae of IAL and free in the nucleus where they associate with nucleoli. Previous histochemical studies (Palanker and Swartz, 1971. Anat. Rec. 169:395) demonstrate the presence of basic proteins in bodies that are similar in size, location and general morphology to both light and dark bodies.

The ultrastructural studies, in conjunction with histochemical studies, suggest a mechanism of nucleocytoplasmic exchange involving IAL in pharyngeal glands of *Ascaris lumbricoides*. It is proposed that light and dark bodies in pharyngeal gland cells contain ribosomal or ribosomal precursor proteins that are produced in the cytoplasm and transported into the nucleus by IAL. Inside the nucleus the ribosomal proteins associate with ribosomal RNA precursors in nucleoli. The structures found in pharyngeal glands of *Ascaris lumbricoides* may be considered either specialized adaptations to functional requirements necessitated by the size of the nuclei or exaggerations of more typical nuclear processes. (This study was supported in part by an NDEA Traineeship and General Research Support Grant 5S01 - RR05375.)

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KOVACS, K. and LONGLEY, J. B., Department of Anatomy, University of Louisville School of Medicine, Louisville, Kentucky. *Composition of basic fuchsin.*

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should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

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dose may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded, in bottles of 100, 500, and 1000. Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, U.S.P., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) **for Injection** may be administered intravenously utilizing 200-400 mcg. of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be given.

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tant biological applications. Among others, it is used in the preparation of Schiff's reagent for the Feulgen, periodic acid-Schiff, and other aldehyde-related procedures, in the Ziehl-Neelsen method for acid-fast bacteria, and in the Gomori aldehyde-fuchsin method that stains various acid glycosaminoglycans and is one of the best techniques for demonstrating elastic fibers. Yet basic fuchsin has no precisely defined composition. It was originally synthesized from aniline and crude toluidines containing both the *o* and *p*- isomers, and as a consequence has a major constituents both rosaniline and pararosaniline, two dyes of definite and different composition. It has been extensively recorded that not all samples of basic fuchsin are equally satisfactory in biological applications. This is particularly true in relation to the Gomori aldehyde-fuchsin method. Ortman *et al.* (J. Histochem. Cytochem. 14:104, 1966) has documented this, and reports that only pararosaniline is the active species in this method. The present study confirms the findings of Ortman *et al.*, and reports on relatively lesser differences in the effectiveness of the two isomers in the Feulgen and periodic acid-Schiff reactions. It further reports studies of procedures for the better characterization of basic fuchsins, indicates recommendations that will be made to the Biological Stain Commission regarding certification of this material.

KWASIGROCH, T. E., Department of Anatomy, University of Virginia, Charlottesville, Virginia. *The effect of vitamin A on the migration of embryonic mouse cells in culture.*

The teratogenic effects of excess vitamin A on embryonic limb development have been reported previously. In this study the behavior of cells in culture derived from limb buds of control embryos was compared with the behavior of cells derived from treated embryos and with cells from untreated limbs cultured in a

medium containing vitamin A acetate. The mesenchymal cells were cultured as small tissue fragments rather than as dissociated cells to avoid the effects of trypsinization. Excised limb buds were separated into proximal (shaft) and distal (autopod) regions. After cutting away the ectodermal covering, the mesenchymal core of each segment was diced into small fragments and cultured on Falcon plastic flasks in Ham's F12 medium supplemented with 10% fetal calf serum. The cells that moved away from the main fragment were observed and photographed using the phase contrast microscope. The rates of movement of the cells were measured from the photographs.

The cells of control proximal segments were bipolar in outline for most of the 3 day culture period, while the shape of cells obtained from control distal segments changed from bipolar to stellate by the 2nd day of culture. The bipolar outline seemed to be a reliable indicator of cells that would actively move in culture. The rates of migration that were calculated showed the more bipolar proximal cells to be more motile than cells from distal limb areas. The presence of vitamin A in the medium affected both the shape and the motility of the cells. Cells became stellate in outline by the end of the 1st day in culture, and the rate of movement of the treated cells of both proximal and distal cultures was much below control levels. The rate of movement in the vitamin A cultures remained suppressed throughout the culture period. In limb fragments of embryos treated in utero with vitamin A (retinoic acid), the cells also showed a decrease in migration tendencies. This effect was observable with 12 hours after seeding. By 3 days in culture the effect of the retinoic acid appeared to wear off and the rate of migration began to increase. These results show that vitamin A impairs those properties of cells necessary for movement and may be important in the origin of limb defects observed after maternal hypervitaminosis

A. (Supported by NIH grant #HD-06550 to Dr. D. M. Kochhar)

LASS, N. J.; KOTCHEK, C. L., and DEEM, J. F., *Oral two-point discrimination: evidence of asymmetry on the right and left sides of selected oral cavity structures.*

The purpose of this investigation was to explore the symmetry of oral two-point limen values on 12 sites in the oral cavity (the midline, right, and left sides of the upper lip, lower lip, tongue tip, and tongue dorsum) and one extra-oral site (finger tip) in each of 14 subjects who had normal oral cavity anatomical structure, speech, hearing, superficial tactile sensation, and neurological history and status. A specially constructed oral esthesiometer was used to obtain subjects' oral two-point discrimination thresholds. A modification of the psychophysical method of limits was employed in establishing two-point thresholds. A total of 10 thresholds, five ascending and five descending, were obtained at each site. It was found that all subjects exhibited evidence of asymmetry in their two-point limen values between right and left sides of at least one of the four oral structures tested. The results provide further support for a proposed theory of "sensory sidedness" as a normal neurological phenomenon of the tactile sensory system.

LU, C. S.; WHEELER, E. J. and McDONALD, Department of Anatomy, Medical College of Georgia, Augusta, Georgia. *Parallel autoradiographic and ultrastructural studies of spinal cord neuroglial elements involved in dna synthesis following sciatic nerve transection.*

Peripheral nerve transection induces proliferation in neuropil of involved brain stem or spinal cord grey matter. Our quantitative studies examine ultrastructure and kinetic behavior of cells proliferating in lumbosacral cord of adult female CBA mice following sciatic nerve transection. Experiment I involved autoradiography

of perfusion-fixed, glycol methacrylate (GMA) embedded cord cross-sections removed 1.5, 2, 3, 4 and 5 days post-transection. Two mice were studied at each interval. H³-thymidine label was injected 12, 8 and 4 hours before sacrifice. Labeled cells appeared in both ventral grey (day 1.5-2) and dorsal grey (day 2 and after). Mean numbers of labeled cells per 3 micron cord cross-section \pm S.E. were 2.6 ± 0.6 , 21.5 ± 0.8 , 12.3 ± 0.5 , 4.6 ± 0.6 and 1.7 ± 0.4 respectively. In Experiment II, mice received doses of H³-thymidine at 36, 40 and 44 hours after transection. Mouse pairs were sacrificed 2, 3, 4, 7 and 15 days post-transection. Mean numbers of labeled cells per 3 micron cord cross-section \pm S.E. were 19.1 ± 0.7 , 28.5 ± 0.9 , 28.5 ± 1.0 , 23.2 ± 0.8 and 6.1 ± 0.7 . Mean grain counts \pm S.E. for these times were 28.1 ± 0.6 , 20.1 ± 0.3 , 20.0 ± 0.4 , 20.2 ± 0.4 and 20.8 ± 0.7 . Significant count reduction occurred before day 3. In Experiment III, 10 mice received H³-thymidine 24, 20 and 16 hours before sciatic transection. Cord labeling did not exceed control levels despite heavy bone marrow labeling.

Ultrastructural study was done on 432 randomly selected cells identified as labeled in parallel epon-section autoradiographs on tissues from Experiments I and II. All labeled cells but 1 pericyte were of the third glial cell type (presumptive microglia). No labeled leukocytes were recognized. Differential counts on ultrastructural features will be presented.

MAUSER, C. C. and ENLOW, D. H., Department of Anatomy, West Virginia University, Morgantown, West Virginia. *Pre-natal growth of the human face.*

This is a study of the remodeling patterns of the fetal facial and cranial bones and a comparison with the postnatal skull. Serial sections of fetal skulls ranging from 8½ to 39 weeks fertilization age were analyzed for resorptive and depository surfaces. These remodeling fields were then mapped for the entire face and

cranial base. The results were then compared with postnatal patterns of growth and remodeling.

Most of the separate bones in the fetal skull begin to remodel when each individual bone reaches a configuration approximating that of the adult. The remodeling patterns of the fetal skull are similar to those of the postnatal skull with three notable exceptions: the anterior surface of the premaxilla, the anterior surface of the zygoma, and the roof of the orbit. The anterior surface of the zygoma and the orbital roof were found to be in a state of transition to the adult pattern, however, in late fetal life. The anterior surface of the premaxilla may also undergo such a transition at a time coinciding with the completion of deciduous eruption.

McCAFFERTY, R. E.; WARD, R. W. and LAWSON, J. M., Departments of Anatomy and Obstetrics-Gynecology, West Virginia University Medical Center, Morgantown, West Virginia.

Histochemical staining of hearts from a select population of human embryos, fetuses, and infants was conducted to study the timing and histologic formation of septal components. Hearts from normal and abnormal concepti of the developmental range of 36 days, in-utero, to 16 days post-partum, including several from confirmed diabetic pregnancies, were fixed with TRIS-Maleic-Buffered Formalin upon acquisition and examined. Alcian blue - PAS - hematoxylin staining was found to be the more productive technique among several.

In the earlier stages of this project, it was reported that the high septal, membranous portion of the I.V. septum nears completion at about the 54th day, whereas at the 58th day a "thumb and finger" grasping of the I. V. muscular septal portion is well established (McCafferty and Ward, Anat. Rec. 175, 2, 509, 1973). In this study the more fibrous septal skeleton including the arterial trunks are compared, macroscopically and microscopically, with the staining characteristics of

the endocardial areas. Affinity of the cardiac tissue for this multiple stain, and most stains, is relatively weak during the first 9 weeks but gradually becomes enhanced and the tissue attains a high affinity by the 19th week. Arterial trunks possess equally an early and continuous blue coloration indicating a strongly positive alcian blue reaction. Cardiac sections derived from concepti of diabetic pregnancies revealed overall reduction in heart size as well as in the constituent parts. In addition, the stain affinity was noticeably reduced throughout the heart sections with less variation from normal appearing in the arterial trunks. (Supported, in part, by U.S.P.H.S.G.R.S. grant 5 S01 RR 05433)

O'STEEN, W. K., Department of Anatomy, Emory University, Atlanta Georgia. *Effects of neonatal androgen on photoreceptor degeneration.*

Retinal photoreceptor damage induced by exposure of albino rats to radiant energy depends on the animal's age at exposure and is more severe after the onset of pubertal changes (O'Steen, Anderson, and Shear, 1974). Recent studies in our laboratory have indicated that removal of the pituitary gland or ovaries "protects" the retina from damage by radiant energy (Olafson, 1974).

At 2 days of age, albino rats were injected with either testosterone propionate (TP, 1.25 mg. s/c) to induce a persistent estrous syndrome in the adult rat, or corn oil solvent. At 12 weeks of age, TP and control rats were exposed either to intense incandescent radiant energy, to destroy the photoreceptors, or to cyclic photoperiod. Rats were autopsied 7 days after exposure, and the eyes were processed to determine the degree of damage.

Exposure to cyclic photoperiod did not substantially alter retinal structure in TP or control rats. On the other hand, exposure to incandescent radiant energy significantly damaged the photoreceptor layer and reduced the overall thickness

of the retina in TP and control groups. However, retinas of TP-treated rats were significantly less damaged than those of control rats, as indicated by a thicker overall retina and the presence of more photoreceptor cells.

These results provide additional evidence of pituitary-gonadal involvement in the progressive development of severe retinal photoreceptor degeneration in response to light exposure.

PLOUMIS, E. and SWANSON, E. A. JR., Department of Anatomic Sciences, Temple University School of Dentistry, 3223 North Broad Street, Philadelphia, Pennsylvania. *Dental roentgenology as a diagnostic tool for systemic arteriosclerosis.*

Clinical observations combined with animal experiments indicate that routine dental radiographs can be used as a simple, non-expensive, screening device for systemic arteriosclerosis.

The animal experiments indicate that the dental pulp is narrowed and that the vasculature of the pulp is comprised under conditions of experimental arteriosclerosis. Human observations in clinic patients tend to confirm these findings. The aging of hard and soft dental tissues will be discussed.

Dental X-rays of humans and experimental rabbits will be presented and discussed. Histologic slides of the dental tissues of the experimental rabbits will be presented, discussed and compared to the human case histories. Data compiled from patient questionnaires will be reviewed and analyzed. Parallels will be drawn between the human and animal results of the experiment.

The conclusion is made that a relationship exists between arteriosclerosis and changes in the dental pulp. It may be possible to diagnose such pulpal changes by dental X-ray and thereby predict the existence of, or the predilection for, arteriosclerosis.

Further reproduction studies in animals are needed to prove the conclusion that arteriosclerosis is familial.

POOLE, M. C.; GREELEY, G. H., JR.; ALLEN, M. B.; MAHESH, V. B. and COSTOFF, A., Department of Endocrinology and Surgery, Medical College of Georgia, Augusta, Georgia. *Pituitary ultrastructure and serum gonadotropins after hypophyseal stalk-section in rats.*

A castrated rat model was developed in which the hypophyseal stalk containing the portal veins was severed surgically and metal foil was inserted to prevent regeneration of the portal vessels. In this model the pituitary no longer has direct communication with the hypothalamus and the only blood supply was through peripheral routes in the dorsolateral regions. The effectiveness of the lesion was demonstrated by very high serum levels of prolactin and very low FSH and LH. Light microscopic examination of the pituitaries from these animals demonstrated a large infarct in the central region of the gland but stainable cells in the peripheral regions. Ultrastructural studies revealed a necrotic central area with abnormal and apparently inactive cells adjacent to it. The cells in the periphery were normal in appearance. Generally, prolactin cells were normal regardless of location and were characterized by a high cytoplasm to nucleus ratio, well-developed rough endoplasmic reticulum, and an abundance of secretory granules. Other cells, especially gonadotropes, had less cytoplasm and were oftentimes devoid of organelles involved in the synthesis and packaging of the hormone. After estrogen treatment the cells were not appreciably changed but after the administration of luteinizing hormone releasing hormone (LH-RH) the gonadotropes were similar to the intact controls. Serum LH and FSH increased after LH-RH administration. When LH-RH was given to estradiol-17 beta primed animals the gonadotropes were normal in appearance and there was an augmentation of release of LH and FSH. Therefore, the administration of estrogen and LH-RH was needed for the gonadotropes of the isolated pituitary to function opti-

mally in the synthesis and secretion of FSH and LH. (Supported by NIH Grant Numbers: HD 04626-13 and HD 00112-06.

RASMUSSEN, N. L.; FRIEDMAN, M. H.; DeNEE, P. B. and SHAW, G. B., Department of Anatomy, West Virginia University, Morgantown, W. Va.; Appalachian Laboratory for Occupational & Respiratory Diseases, National Institute for Occupational Safety and Health, Morgantown, W. Va.; Suite 703, Medical Tower, Jackson, Mississippi. *Bronchiolitis fibrosa obliterans: case study via transmission electron microscopy.*

Bronchiolitis fibrosa obliterans is a rare pulmonary disorder showing as a primary characteristic, obliteration of the terminal and respiratory bronchioles by a mass of polypoid fibroblastic granulation tissue. A survey of the literature has revealed no previous study of bronchiolitis fibrosa obliterans using the transmission electron microscope.

The tissue for this study is from a subsegmental resection of the right lower lung lobe of a 56-year-old white male who was exposed to burning jute-bagged cotton approximately five months prior to the biopsy. The tissue has been fixed initially in a 10% formalin solution and approximately six months later reprocessed for electron microscopy.

Light microscopy shows connective tissue nodules surrounded by atelectatic lung infiltrated with numerous lymphocytes, macrophages, and leukocytes. The nodules appear similar to the nodules observed in the pathology of silicosis and are differentiated from the latter only with difficulty.

An electron microscope photomontage of a nodule reveals fibers (125 to 900 Angstroms in diameter) and fibroblasts in an amorphous ground substance. The relative amounts of fibrous material versus ground substance, as well as the appearance of the fibroblasts, confirms this as mesenchymal connective tissue.

In addition to the nodular mesenchymal connective tissue, similar but less organized patches of this same tissue are seen

dispersed through the parenchyma, and in at least one instance, in the lumen of a capillary. Numerous macrophages are associated with this mesenchymal connective tissue infiltration.

This ultrastructure study shows that there is clearly an obliteration by mesenchymal connective tissue of the peribronchiolar alveoli and capillaries in bronchiolitis fibrosa obliterans. This heretofore undescribed involvement supplements the previously recognized bronchiolar pathology.

Since there have been no previous transmission electron microscopic studies of bronchiolitis fibrosa obliterans, this study provides a fundamental ultrastructural characterization of this disease. In addition, combined with the previous scanning electron microscopy by DeNee et al,¹ for the first time a documented case of bronchiolitis fibrosa obliterans has been characterized by both SEM and TEM to be associated with the presence of silica, although this in no way implies a cause/effect relationship.

¹ DeNee, P. B.; Abraham, J. L.; Gelderman, A. H.: SEM identification of biogenic silica in jute: silica in human lung following exposure to burning jute, Abstract 10A, Ninth Annual Conference of Microbeam Analysis Society, Carlton University, Ottawa, Canada, July 1974.

REYER, R. W., Department of Anatomy, West Virginia University, Morgantown, W. Va., *Availability time of ³H-thymidine in newt eyes following intra-peritoneal injection.*

In order to follow cells over a period of time after labeling with ³H-thymidine, it is necessary that the isotope be available for only a brief exposure period so that there is no recruitment of additional labeled cells to the original population. To test the duration of this availability time in adult newts, ³H-thymidine (1-1.5 uCi/gm. body wt.) was first injected into the host. Then donor, regenerating lenses were implanted into host, lentectomized eyes at consecutive intervals of time for two weeks after isotope administration. The eyes were fixed from two hours to 24 days after operation and studied in

radioautographs. Regenerating lenses, exposed to the isotope for two hours beginning 40 and 80 minutes after its injection, were labeled while those implanted three to 20 hours after injection were unlabeled. Except for one animal, there was no labeling of implants if they remained in host eyes for one or two days beginning one to 14 days after injection. However, when regenerating lenses were placed in host lentectomized eyes one day after injection and fixed from one to 24 days later, four out of 22 implant and two out of 14 host, regenerating lenses were distinctly labeled and 14 implant and 7 host, regenerating lenses had a very light label. Therefore, a true "pulse" label is not obtained in adult newts under these conditions. (Supported by Research Grant EY00196 from Nat. Eye Instit., N.I.H.)

ROSENQUIST, T. H., and TROYER, H. Medical College of Georgia, Department of Anatomy, Augusta, Ga. *The effect of cetylpyridinium chloride fixation on alcian blue staining.*

The protein portions of the stroma are fixed by standard aldehyde fixatives; whereas, the mucopolysaccharides (MPS) are not fixed but are lost into the aqueous fixative solutions. Retention of the MPS can be accomplished readily by including the quaternary ammonium salt cetylpyridinium chloride (CPC) in the aldehyde fixative (Sobin and Rosenquist, *Microvascular Res.* 5:271).

It has been reported that CPC interferes with the effectiveness of staining of the dye Alcian blue 8GX, which we have used frequently according to the method of Scott and Dorling (*Histochemie* 5:221). Since this procedure is most useful, and since we use CPC to preserve MPS, therefore we tested the interference hypothesis.

Costal cartilage from a 57-year-old male was fixed in formalin/CPC: and in a nonaqueous fixative as a control. Tissues from both fixatives were stained in Alcian blue 8GX and stain intensity was determined by measuring alcianic copper with atomic absorption spectrophotometry.

(Rosenquist and Rosenquist, *J. Histochem. Cytochem.* 22:104).

No difference was found, indicating that no interference in Alcian blue staining results from CPC fixation of stromal MPS.

SADLER, T. W., Department of Anatomy, University of Virginia, Charlottesville, Virginia. *The teratogenic activity of chlorambucil in the mouse: an in vivo and in vitro examination.*

The occurrence of congenital malformations has been reported in animals after treatment with some difunctional alkylating agents. Chlorambucil was used in this study to: 1) confirm its teratogenic activity in mice; 2) to establish its ability to interfere with organogenesis directly in organ culture; 3) to study its role in the production of limb defects.

Pregnant mice of ICR/DUB strain were given single oral injections of chlorambucil (20 ug/g or 14 ug/g body weight) on the 10th, 11th, 12th, or 13th days of gestation. Fetuses, examined on the 18th day exhibited tail, cranial, and limb defects as well as growth retardation. The type and frequency of malformations were related to both the dose and the day of treatment. Limb defects occurred in fetuses treated on the 11th or 12th day of gestation (plug day = 1st day), while tail defects were observed on all days with the greatest incidence occurring on the 11th day. Cranial abnormalities were found only in the most severely affected litters.

Chlorambucil was found to be very effective in *in vitro* experiments. Limb buds were isolated from untreated 12th day embryos and cultured in serum supplemented BGJ medium to which chlorambucil was added in doses of 0.5, 1.0 1.5 and 2.0 ug/ml. Limb development was retarded in all treated cultures and cartilage abnormalities were observed. The extent of deformity was dose related.

In the next series of experiments, pregnant animals were treated with teratogenic doses of chlorambucil on the 11th day of gestation. Limb buds were isolated from

the embryos 24 hr. later and cultured in control medium. These limb buds continued to exhibit growth impairment and cartilage abnormalities. Further work toward determining the structural (EM) and metabolic basis of the observed defects is in progress. (Supported by Pharmaceutical Manufacturers Association Foundation and NIM grant #HD-06550 to Dr. D. M. Kochhar)

SANNES, P. L., and HAYES T. G., Department of Anatomy, The Ohio State University, Columbus, Ohio. *Ultrastructure of parathyroid gland of the mongolian gerbil.*

The parathyroid gland of the gerbil was a bilateral, cervical organ found adjacent to the thyroid gland. It possessed a typical connective tissue border. A polygonal or elongated chief cell was the single cell type recognized, which was arranged in groups as cords or sheets. The chief cell had two different cytoplasmic densities as revealed by electron microscopy. Generally the dark or more electron dense cell was characterized by highly interdigitated cell borders, large numbers of mitochondria, and a relatively high concentration of organelles associated with protein and carbohydrate synthesis. This was in contrast to the light or more electron transparent cell which typically had little or no complex intercellular interdigitations, fewer mitochondria, a smaller relative complement of organelles, and frequent lipid bodies within the cytoplasm. These comparisons suggest that the dark cell was the more active of the two states defined. However, definitive separation was made difficult by the presence of cells which appeared to possess characteristics of both states, and were thus classified as "transitional." Mitochondrion—rich oxyphil cells, water clear cells, or their likeness were not observed.

Three distinct Golgi-related vesicle populations were recognized. The first, a large, smooth-surfaced vesicle was suggested to be a prosecretory granule. Within its membrane border was displayed a

typical halo-like appearance about a variable amount of particulate material, similar to that observed in several other vertebrate species. The second was a small, coated vesicle which was occasionally observed intimately associated with the prosecretory granule. In addition, this vesicle was observed in pinocytotic-contact with the plasmalemma. It was proposed that the coated vesicle could represent a condensing-concentrating vesicle. The third was a small, smooth surface vesicle which was slightly more electron dense than the background cytoplasm. Its function was not discernable.

The mature secretory granules observed were not unlike those found in other vertebrate species. They were very electron dense and were enveloped by a smooth membrane.

SEVERIN, C. M.; MASSOPUST, L. C., JR. and YOUNG, P. A., Department of Anatomy, Saint Louis University, St. Louis, Missouri. *Pallidothalamic projections in the rat.*

Sterotaxic electrolytic lesions were placed in the intermediate and posterior portions of the pallidum in one group of albino rats. The pallidothalamic projections were studied with the Fink-Heimer technique and were verified by autoradiography in another group of animals injected with tritiated leucine. Nissl stained sections of the thalamus were used to delineate the thalamic nuclei into the ventral nucleus (VE), ventral nucleus pars anterior (VA), ventral nucleus pars medialis (VM), ventral nucleus pars dorsalis (VD), and the reticular nucleus (RT) according to Pellegrino (1967).

The results demonstrated that pallidothalamic fibers coursed through the ipsilateral internal capsule. These fibers appeared in fascicles coursing medially and interdigitating with the capsular fiber bundles. As the pallidal fibers passed through the reticular nucleus some appeared to terminate, but the majority continued through the external medullary lamina to enter the ventral nuclei men-

tioned above. Terminations appeared to be limited to the ventral part of the VE, but were uniformly distributed throughout the VA, VM, and VD. Terminations were not observed in the corresponding contralateral nuclei.

SHEETZ, J.; MENAKER, L; COBB, C., Department of Anatomy and the Institute of Dental Research, University of Alabama in Birmingham, Birmingham, Alabama. *Morphological and salivary alterations in developing submandibular gland of isoproterenol (ISP) treated rats.*

The sympathomimetic drug ISP has been shown to induce morphological and salivary alterations in rat submandibular salivary glands (Lab. Invest. 30, 1974). However, the sequence of changes within the gland which result in such alterations have not been thoroughly investigated in the developing gland. The purpose of this study was to determine the time required for the appearance of morphological and salivary changes in developing submandibular gland of ISP treated rats. Postnatal rats 5 days of age received 16 mg/kg of ISP twice daily. Pilocarpine stimulated saliva and samples of salivary gland tissue were collected after one, two, three, and four days of treatment. Control samples were taken from animals receiving no treatment. Acrylamide gel electrophoresis of whole saliva demonstrated a large mobile (LM), imido black positive band in samples from animals receiving ISP for as little as 2 days. This band did not appear in control samples. Morphological changes in the gland also became evident after 2 days of treatment. In addition to terminal tubule and proacinar cells, large acinar cells containing light staining, electron lucent granules become evident. In comparison gland acini from control animals contained terminal tubule and proacinar cells. These results demonstrate the rapid onset of ISP induced functional and morphological changes seen in the developing rat submandibular gland. (Supported by N1AMDD Grant #70246)

STURTEVANT, R. P., Department of Anatomy, Northwestern University Medical School, Chicago, Illinois. *Changes in human circadian rhythms during simulated and actual transmeridial displacement.*

The effects of both simulated and actual geographical displacement over several time zones was assessed as changes in AUTORHYTHMOMETRIC measurements. Blood pressure, oral temperature, an evaluation of mood and vigor, and performance of eye-hand coordination, manual dexterity, and speed and accuracy in adding and memorizing numbers were recorded several times at random intervals during each of 72 consecutive experimental days. Five simulated time zone shifts were made during the first 35 days. The transition from Central Standard Time to Europe time was accomplished by arising and retiring one hour earlier each day for six days (a 6-hour phase advance). This was immediately followed by an hourly (phase) delay in wake and sleep times for each of six days—thus a transition from Europe time to Central Standard time. An actual flight from Chicago to Europe and return was followed by additional simulated time zone changes.

Although the author experienced greater discomfort and intensity of disrhythmic symptoms ("jet lag") during the simulated and actual west-to-east travel (phase advance) than in the reverse direction, a well-defined, statistically significant body temperature rhythm was evident only during the periods of phase advancement. The rhythm was lost during phase delays and during most of the time following the actual flight to Europe.

Due to a learning trend that occurred during the first five weeks, performance data of manual dexterity and eye-hand coordination exercises need to be distinguished from the learning trend by appropriate statistical techniques.

TROYER, H. and ROSENQUIST, T., Department of Anatomy, Medical College of Georgia, Augusta, Georgia. *Quantitation*

of histochemical staining intensities with photographic silver analysis.

A method has been developed for quantitating histological staining intensities by obtaining photographic negatives and measuring the silver concentration. It has been shown that when the log of the exposure time is plotted against the silver concentration in the negative, a sigmoid curve is obtained with a rather straight middle segment (Hurter-Driffield curve). It was necessary therefore to design the experiment such that all the values fell within the straight segment. A Nikon SKe microscope with a Microflex AMF photographic attachment was used. The conventional transformer was replaced with a constant voltage power supply. The photographic conditions and development of the negatives were carefully standardized. A small disc was punched out of each frame with a paper punch. The silver was eluted with 1 ml of 35% nitric acid for 2 hours and the silver content measured with an atomic absorption spectrometer. The accuracy of the method was tested by analyzing the density of a series of stained costal cartilage sections whose density had been previously determined with a microspectrophotometer. The data were reproduced with reasonable accuracy. Densitometric data can be obtained in this way with a minimal investment in equipment.

WAGGONER, P. R. and REYER, R. W., Department of Anatomy, Wayne State University, Detroit, Michigan, and West Virginia University, Morgantown, West Virginia. *DNA synthesis during lens regeneration in larval xenopus laevis*.

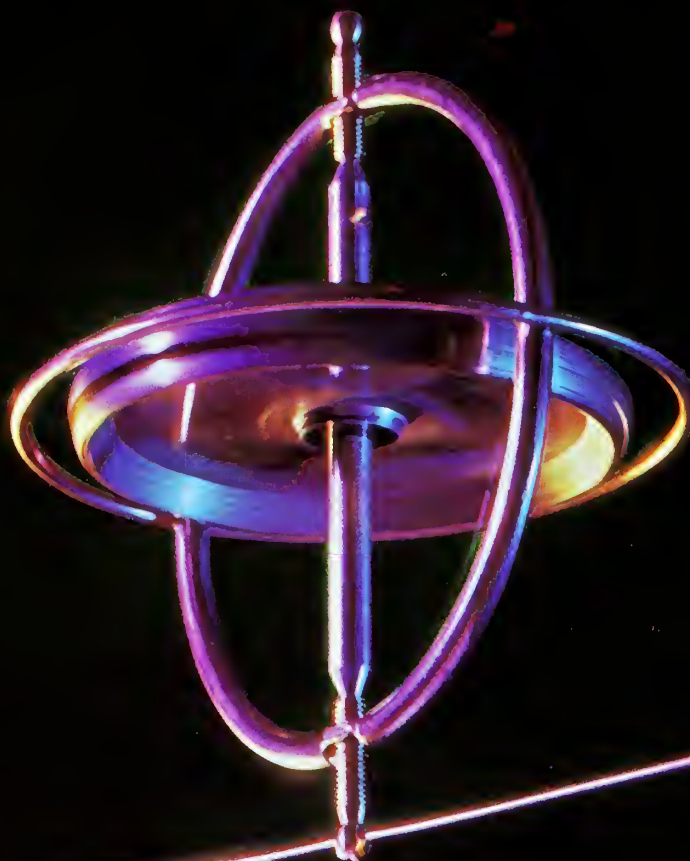
Larvae of *Xenopus laevis* at stages 50-53 (Nieuwkoop and Faber) were lentectomized and then injected with tritiated thymidine at various times after lentectomy. In Series I, the animals were injected 1, 2, 3, 4, 6, 8, 10, 12, 15 or 17 days after lens removal and fixed three hours after injection. Autoradiographs of serial cross sections through the eyes were prepared. Increased incorporation of H³-

thymidine in the cells of the regenerating lens was first observed two days (stage 2 of Freeman) after lentectomy. All the cells of the lens vesicle incorporated H³-thymidine until stage 4 at which time the cells in the inner wall of the vesicle began to differentiate into lens fibers. Labeling then became restricted to the peripheral cells (prospective lens epithelium and prospective lens fibers). At stage 5 of regeneration, H³-thymidine incorporation became restricted to the lens epithelium. In Series II, animals injected three or four days after lentectomy were fixed daily, one through seven days after injection. Many stage 3 and stage 4 regenerates were recovered with label throughout the lens vesicle. Stage 5 regenerates which were found seven days after injection had label over lens fibers as well as over the lens epithelium. (Supported by Research Grants EY00196 from Nat. Eye Instit., N.I.H. to W.V.U. and Gen. Res. Grant RR-5384-12 from N.I.H. to Wayne State Univ.)

WALKER, E. R.; FRIEDMAN, M. H.; OLSON, N. O. and SAHU, S. P., Department of Anatomy, and Division of Animal Veterinary Science, West Virginia University, Morgantown, West Virginia. *Avian arthritis—a model for rheumatoid arthritis*.

It is widely hypothesized that human rheumatoid arthritis is initiated by a virus or other infectious agent provoking a chronic inflammation of the synovium. Little progress is being made either to prove or disprove this idea, since an infectious agent has never been isolated in man. The pathology of the avian viral arthritis, a disease of poultry, resembles the pathology seen in human rheumatoid arthritis, so that this naturally occurring avian arthritis fulfills the requirements of an experimental model for the study of human rheumatoid arthritis.

Birds were inoculated with the avian reovirus (strain WVU 2937) which was originally isolated from hock joints of arthritic birds and proven to be the causa-



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tive agent of the arthritis.¹ The synovium was studied with transmission and scanning electron microscopy. Serological techniques were used to study sera collected from these birds.

Virus replication was demonstrated in fibroblasts of the subsynovium four days post-inoculation. No replication was observed at any time in the closely-packed synovial lining cells.

Whereas most studies related to rheumatoid arthritis focus primarily on the synovial lining cells and are undertaken at a late stage of the disease, this study suggests that it may be important to look at the subsynovial tissue earlier in the disease. By eleven days post-inoculation, these inflammatory changes could be seen in the subsynovium: infiltration by plasma cells and lymphocytes; sequestration of inflammatory debris by macrophagic cells; obliteration of synovial blood vessels, a sign of interference with microcirculation in the joint. The majority of the thirty-five birds in this group recovered from the viral arthritis, did not become crippled and did not show long term involvement of synovium and cartilage that had been observed in previous experiments done by Kerr and Olson.²

However, in a mixed infection experiment where forty birds were inoculated with the virus and another arthritis-causing micro-organism *Mycoplasma synoviae*, the majority of the birds became crippled, showing severe involvement of the synovium and articular cartilage over a six month period. In addition, several birds showed a high titer in a test for rheumatoid factor, a large antibody found primarily in serum of rheumatoid arthritis patients.

1. Olson, N. O., Shelton, D. C., Munro, D. A.: Infectious synovitis control by medication—Effect of strain differences and pleuropneumonia-like organisms. *Am. J. Vet. Research* 18, 735 (1957).
2. Kerr, K. M. and Olson, N. O.: Pathology of chickens experimentally inoculated or contact-infected with an arthritis-producing virus. *Avian Diseases* 13, 559 (1967).

WARD, R. C.; VOLCAN, I. J.; MAHESH, V. B.; ALLEN, M. B. and COSTOFF, A., Departments of Endocrinology and Surgery, Medical College of Georgia, Augusta, Georgia. *Ultrastructural studies of somatotropes and mammotropes in primate pituitary glands.*

The ultrastructural identification of somatotropes and mammotropes in rat anterior pituitary glands has been established and generally acknowledged. However, whether one or two cell types are responsible for the secretion of growth hormone (GH) and prolactin (PRL) in primates is controversial. It has previously been established that each tropic hormone is associated with a population of secretory granules of a specific maximum diameter (Costoff and McShan, 1969). Ultrastructural studies were conducted on pituitary glands from untreated male and female rhesus monkeys, pregnant animals, and in those bearing renal autografts of the pituitary gland. Serum prolactin levels are known to be high during pregnancy and in monkeys containing renal autografts. Two distinct cells containing large granules were identified. Type I cells contained granules of 400 mu maximal diameter and were more conspicuous in male monkeys. Type II cells were more abundant in female animals and had granules that measured up to 800 mu in diameter. In pituitaries from pregnant monkeys and those from renal autografts, type II cells predominated indicating that these cells secreted PRL. Human pituitaries were obtained from acromegalic patients without lactation that exhibited high serum levels of growth hormone and it was found that type I cells predominated. It is concluded that type I cells secrete growth hormone and type II prolactin. Both cell types were present in infant monkey pituitary glands suggesting that the type II cell was not a variant of the type I cell. The results indicate two distinct cell types, one that produces GH and the other PRL in primates. (Supported by NIH Grant Number: HD 00112-06.)

WESP, R. K.; GOODMAN, I. J. and LATTAL, K. A., Department of Psychology and Department of Behavioral Medicine and Psychiatry, West Virginia University, Morgantown, W. Va. *Paleostriate and parolfactory destruction and some effects upon behavior in the pigeon.*

A study of the possible functions of two basal forebrain zones, lobus parolfactorius (LPO) and paleostriatum (PC), considered by many until recently as a unified structure, was carried out in the pigeon. Following initial behavioral training on a fixed interval schedule of reinforcement, birds were surgically treated by stereotactically-placed electrolytic lesions (bilaterally) in either PC or LPO. A sham-operated group served as controls. Following surgery, subjects were tested daily for three additional weeks. Four daily behavioral extinction sessions followed. LPO subjects showed the most severe

behavioral disruption which involved a significant deficit in response rate and timing ability during the first two post-surgical weeks, an initially-lowered response rate during extinction and marked defensive reactions to stimuli. PC subjects also showed early severe response depression and timing deficits following surgery which appeared to approach normal levels after 5-7 days and an initial increase in response rate during extinction. All PC birds appeared quite somnolent for the first 3-5 post-operative days with three of these subjects showing continued somnolence throughout the remainder of the experiment. Histological analysis revealed that the latter had received more caudal PC lesions than the other PC subjects. These results were discussed in terms of possible influences of descending fore-brain pathways on behavior.

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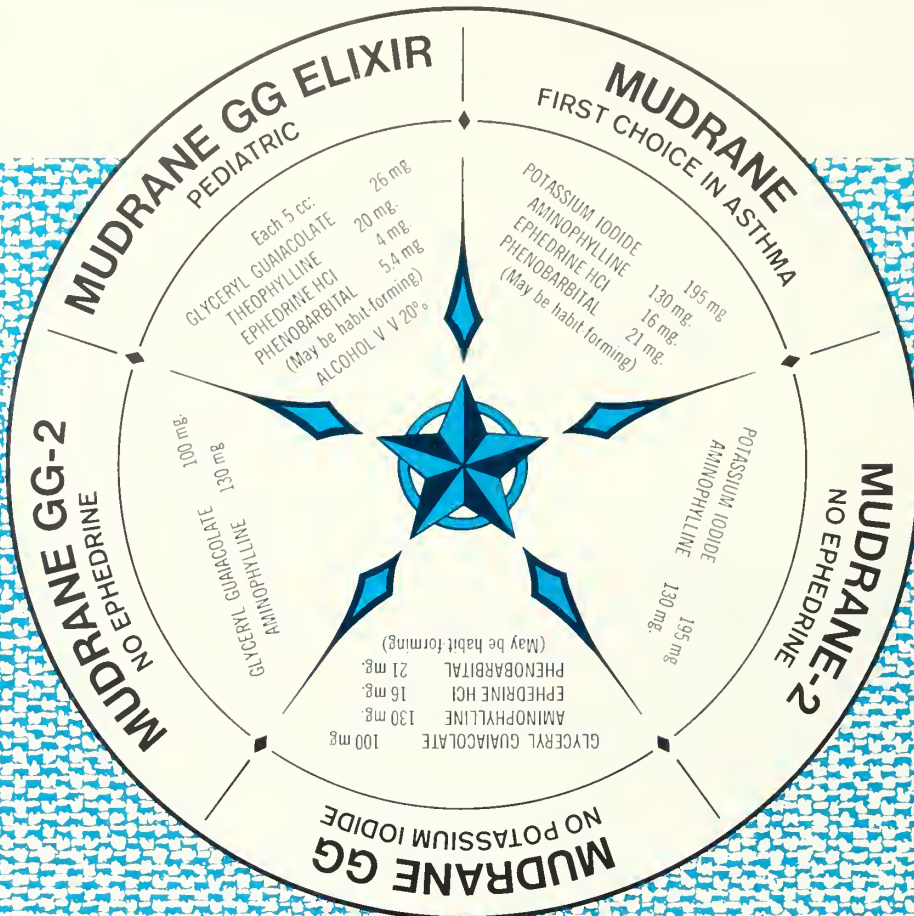
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CONTRAINDICATIONS: Aminophylline/Theophylline is contraindicated in the presence of severe cardiac arrhythmias and patients with massive myocardial damage. Ephedrine, in presence of severe heart disease, extreme hypertension and in hyperthyroidism. Phenobarbital, in porphyria and in patients with known phenobarbital sensitivity. Potassium Iodide, in pregnancy (to protect the fetus against possible iodine-induced depression of thyroid activity), in tuberculosis (produces gumma dissolution), and in acne; also in the presence of known iodide sensitivity. **PRECAUTIONS:** Aminophylline/Theophylline should be avoided in patients with massive myocardial damage and/or severe cardiac

arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdose. Potassium Iodide: Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing anginal pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdose. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

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What Has the AMA Done for You Lately?

In recent weeks this has been a question that probably all doctors in South Carolina have been asking themselves. The threat of a \$90 a year dues increase which finally terminated in a compromise \$60 temporary assessment for 1975, has left many doctors asking this question. Is the AMA worth the money? This is a serious question; and it deserves a serious and thoughtful answer. Walk in any doctor's dressing room and you can be regaled with countless stories about the ineptitude and the stupidity of the AMA. On a few occasions I have been very unhappy with them myself. Yet we must remember that the AMA is composed of doctors and run by doctors. Doctors are human beings and are open to honest error just as other human beings. Probably the greatest evil of the AMA is a necessary one—its very size. Like the diplodocus of the prehistoric Jurassic era, communication is often slow between the brain and the tail. Yet on many occasions, I have been amazed at how quickly and effectively this tough old dinosaur could move. Despite the attractiveness, the volume, and the genuine merits of the content of its publications, communications is probably still the greatest problem of the AMA. I say this because I believe that very few physicians fully realize all that the AMA does for them, whether they are a member or not.

Even if you are not a member of the AMA, you benefit from the way it works on the behalf of the profession to insure quality medical education and care. 1) As a member of the Commission on Continuing Medical Education, the AMA participates in accreditation of medical schools and the review and certification of internship and residency programs. 2) As a member of the Joint Commission on Accreditation of Hospitals, the AMA shares the responsibility for the accreditation of hospitals and other health care facilities and services. 3) It accredits schools and training programs for allied health personnel. 4) It assists in the development of continuing education study programs in every branch of medicine. It originated the Physician Recognition Award, which has been widely imitated by other medical specialty societies. 5) It is the guardian of medical ethics and has participated in the development of various review committees and medical staffs. 6) It sponsors or co-sponsors more than 1,000 meetings and medical and health study sessions every year.

One of the many false accusations against the American Medical Association is that it serves only the selfish interests of doctors and does not care for the welfare of the general public. The absurdity of this accusation becomes apparent when you consider that among the few innovative and ongoing programs the AMA has developed for improved health care in America are included: 1) Model school health screening programs; 2) Model emergency medical service for the nation's airports; 3) Model drug abuse programs for local communities; 4) Innovative rural health care delivery systems;

5) Pilot nutritional educational program for the poor; 6) New approaches to health care delivery for the poor; 7) Exploration of environmental, occupational health problems, and development of solutions; 8) Distribution of over 10 million pieces of health education literature to the public, schools, public health agencies; 9) Investigation and exposure of quacks and quack products; and, 10) Guidelines for comprehensive emergency medical care systems, the training of ambulance personnel, and categorization of hospital emergency care capabilities.

Many people have accused the AMA of a negative attitude toward legislation and always being against any progressive legislation. The fact is that the AMA has initiated and supported at least 3 bills for every 1 it has opposed. Among this recent positive legislation sponsored by the AMA are included the Indian Health Care Improvement Act, National Health Service Corps, the Drug Abuse Education Act, the establishment of community mental health centers, the extension of the maternal and child care health program, the Communicable Disease Control Act, the Allied Health Training Act, the Act for Better Drug Labeling, the Act for Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment, and Rehabilitation.

Among the key benefits and services available to the membership are: 1) Insurance programs that can provide broader coverage at lower costs including the excess major medical program, the group term life insurance program, the supplemental "in hospital" insurance, the accidental death and dismemberment plan, and disability income insurance; 2) The AMA operates the nation's largest physician placement service; 3) It is the leader in scientific publications with the JAMA and numerous specialty journals; 4) It provides authoritative legal information and guidelines on every aspect of practice of medicine; 5) It provides professional management information and guidelines to increase the productivity and profitability of your practice; 6) It offers the research resources of one of the nation's greatest medical libraries and film libraries.

Despite accusations of being large and cumbersome, the AMA has provided long and short term benefits for all physicians in the United States. As a long term example, more than 20 years ago the American Medical Association led the way to correct the inequities of our tax structure so that self-employed individuals could set aside each year a specific amount of money for retirement purposes. Income tax on the money was to be deferred until drawn from through an appropriate pension plan. This plan had been in existence for corporations since 1942, but was not allowed to the self-employed. After a period of 8 years of very intensive effort, and with considerable financial backing of the American Medical Association and other groups, the Self-Employed Individual Tax Retirement Act was passed by Congress and was signed into law. This law provided the self-employed with a yearly deduction of contributions on their own behalf of up to 10% of earnings or \$2,500, whichever was smaller. The income on this money was to be tax deferred until distributed at the time of retirement. Former Congressman Eugene Keogh of New York was instrumental in this legislation, and the law still carries his name. Similar efforts by the AMA obtained reluctant recognition from the IRS for Professional Associations. In 1964, Congressman Keogh introduced legislation which would have repealed the 10% or \$2,500 limitation of self-employment plans. Although this legislation was defeated at that time, it was strongly supported by the American Medical Association. Now, some 10 years later, through the relentless efforts of the American Medical Association to increase the amount and percentage of physician's income to be deferred, this legislation has finally become law. It liberalized existing Keogh provisions for increase in the annual limits of contributions made to retirement plans to 15% of earned income or \$7,500, whichever is less.

What does this mean to the self-employed physician? It means that individual doctors or unincorporated partnerships will be able to make deductible contributions of up to \$7,500 a year to retirement plans which are approved by the Internal Revenue Service. Income tax on this amount is to be deferred until withdrawal. For example, suppose an individual were in the 40% tax bracket during the time he was contributing to a retirement fund and in the 20% bracket during his retirement years. This one persistent effort on the part of the American Medical Association would save that individual \$1,500 a year. Savings made by taking advantage of this legislation, regardless of income in itself, would be far in excess of any dues or contributions made by an individual as a member of the American Medical Association.

A short term example of the benefits of the effort and leadership of the American Medical Association is that in opposing Phase IV economic controls on physicians and hospitals and vigorously objecting to the extension of the Economic Stabilization Act beyond April 30, 1974, which would have retained controls on health, medical and hospital services. The AMA filed suit against the Cost of Living Council on February 19, 1974, to seek an end to economic controls on physicians. This suit charged that Phase IV regulations were confiscatory, arbitrary and capricious. The AMA was represented on the Health Industry Advisory Committee of the Cost of Living Council and although the committee opposed Phase IV and extension of the Economic Stabilization Act, it became necessary for the AMA to convince members of Congress that this act should be permitted to expire as of April 30th. The Senate Banking, Housing, and Urban Affairs Committee tabled proposals which would have extended the program, and so has the House Banking and Currency Committee.

Just before elections this past year, the Kennedy Manpower Bill (S3585) had provisions which would have given the federal government power of relicensure and recertification, put medicine under a utility concept with regulation for fees and services, and given the Secretary of Health, Education and Welfare the power to determine the number of internships and residencies to be approved and where graduates of medicine could practice. The determined efforts of the AMA stripped this bill of these odious provisions. These are two short term examples of the beneficial influence of the AMA.

At this point some wise guy always says, "Why should I join the AMA? Somebody else will always pay their dues, and I can get all these benefits for nothing." We have all met people like this. He is the guy who borrows broke money from some kindhearted chump in a poker game, uses it to break the chump, and then brags about it. He is the guy who complains about the noise of your lawnmower, but always seems to need to borrow it from you. He's the guy that always has the urgent call of nature when your large group at dinner is settling the check with the waiter. In gambling circles he is sometimes called a hustler, but is usually referred to as a chisler. If enough doctors "let George do it," the AMA will quietly disappear. Most doctors I know would rather pay their way, if they know what they are getting for their money. I think the AMA offers a lot for your money.

Donald G. Kilgore, Jr., M.D., President
South Carolina Medical Association

50 YEARS AGO

January 1925

This issue carried a two page advertisement for the Gilchrist Chlorine Ejector, an apparatus with which the physician could set up his own gas chamber. The

only indication for its use was the offer of a booklet called "The Use of Chlorine Gas in Certain Respiratory Diseases." The safety of the ejector was emphasized strongly.

If you want the health coverage chosen by more South Carolinians

Blue Cross is what you need.

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**Blue Cross[®]
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Putting out the fires of arthritic pain

Rheumatoid arthritis can sometimes spread like wildfire, with joint after joint going up inflamed. The usual onset is manifested by spotty joint involvement but an acute onset of symmetrical polyarthritis may be noted.**

If aspirin fails, consider Butazolidin alka. Giving one capsule four times a day often provides prompt, pain-relieving, anti-inflammatory action to help restore joint mobility. The results you can get within a week can be maintained on as little as one or two capsules daily.

Serious side effects can occur. Select patients carefully (particularly the elderly) and follow them closely in line with the drug's precautions, warnings, contraindications and adverse reactions. For full details, please read the prescribing information. It's summarized on the back of this page.

Butazolidin® alka

Each capsule contains:
100 mg. phenylbutazone USP
100 mg. dried aluminum hydroxide gel USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.



**Fire fighter
for arthritic
flare-ups.**

Butazolidin® alka

Each capsule contains:
100 mg. phenylbutazone USP
100 mg. dried aluminum hydroxide gel USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.
Ragan, C. The Clinical Picture of Rheumatoid Arthritis, in Arthritis, ed. 8, edited by J. L. Hollander and D. J. McCarty, Jr., Philadelphia, Lea & Febiger, 1972, chap. 21, p. 335.

Geigy

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of fever, sore throat, oral lesions (symptoms of blood dyscrasia), dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications: Children 14 years or less, senile patients, history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy, blood dyscrasias, renal, hepatic or cardiac dysfunction, hypertension, thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals. Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug, its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.

(B)98-146-070-J (10/71)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardley, New York 10502

BU 10259

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (> 5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F CO.
Carolina, P.R. 00630
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SmithKline Corporation

KEEP THE HYPERTENSIVE PATIENT ON THERAPY KEEP THERAPY SIMPLE WITH **DYAZIDE**[®]

Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

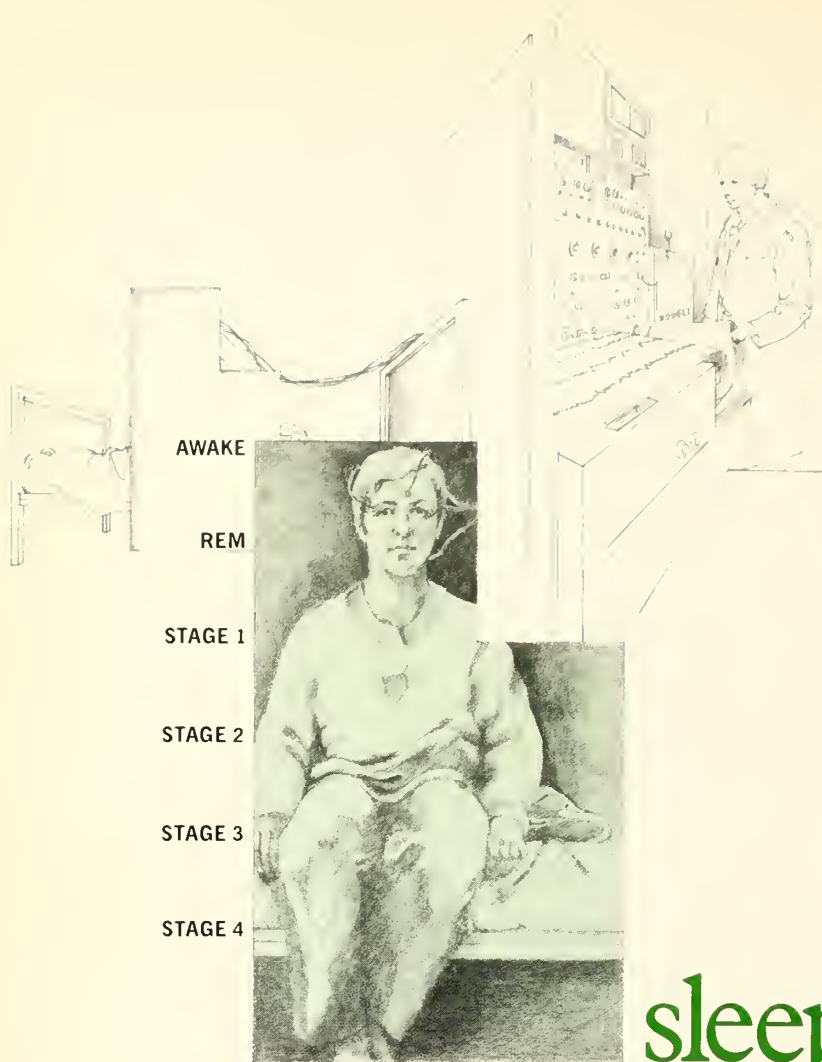
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Just 'Dyazide' once daily or twice daily
No inconvenient potassium supplements
Nor special K⁺ rich diets needed as a rule



Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP

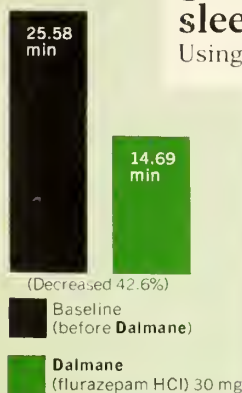


sleep
begins within
17 minutes, on average ...
an initial benefit of

Dalmane[®]
(flurazepam HCl) proved by a
**22-night clinical study of insomnia patients
in the sleep research laboratory and at home¹**

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.¹

Average Time Required
to Fall Asleep (4 Studies,
16 Subjects²⁻⁵)



confirmed by clinical studies in four geographically separated sleep research laboratories²⁻⁵

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage²⁻⁵

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

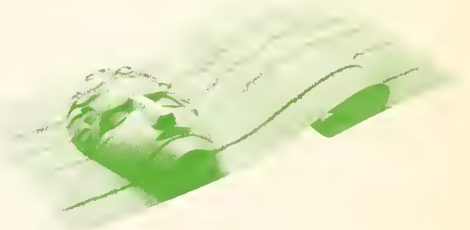
Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.



when restful sleep
is indicated

Dalmane[®] (flurazepam HCl)

One 30-mg capsule h.s. — usual adult dosage
(15 mg may suffice in some patients).

**One 15-mg capsule h.s. — initial dosage for
elderly or debilitated patients.**

- induces sleep within 17 minutes, on average
- reduces nighttime awakenings
- sustains sleep 7 to 8 hours, on average, without repeating dosage



ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

REFERENCES: 1. Kales A, et al: *Arch Gen Psychiatry* 23:226-232, Sep 1970

2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971

3. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

When diarrhea has his number...



Lomotil puts him back in the game.

Physicians and patients both want prompt control of the symptoms of diarrhea. A rapid, uncontrolled loss of fluids and electrolytes can cause a medical crisis, particularly in children, and in patients who are seriously ill, or in people who are badly undernourished.

Lomotil usually stops diarrhea promptly. This rapid action halts the emergency aspect of diarrhea

and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate antibiotic therapy should be given along with Lomotil.

Lomotil has few side effects, and those that do occur are generally mild.

Lomotil[®]
TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride 2.5 mg.
(Warning: May be habit forming)
atropine sulfate 0.025 mg.

Usually stops diarrhea promptly.

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdose or individual hypersensitivity, reactions similar to those after meperidine or morphine overdose may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdose; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoons (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdose: Keep the medication out of the reach of children since accidental overdose may cause severe, even fatal, respiratory depression. Signs of overdose include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
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454 R

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Editorials

A Mid Winter of Discontent

Perhaps it was the "flu bug" which has been lingering around the upper nasal passages for the last six weeks, or perhaps it was the economic spector we face, or perhaps it was the coaching fiasco at one of our state institutions, certainly it was not the great weather and hospitality at the "Port City" nor the lovely reception at the Gibbes Art Gallery, but for some reason we came away from the 1974 Mid Winter meeting of SCMA with a feeling of discontent. This was in marked contrast to the buoyancy and hope that we felt after the 1973 Mid Winter meeting. Let me relate to you some of the reasons for this discontent.

1. The condition of the AMA (see following editorial for details).

2. Impotence of SCMA and organized medicine to deal with marginal and dangerous practitioners of medicine.

Over the past few years several instances of doctors whose level of competence was below tolerable have been brought to the attention of SCMA leadership, but our organization has been powerless to deal with these situations. The continued practice by these physicians presents a danger to patients and an insult to our profession. We will make some suggestions for a possible remedy to this situation in a later issue of JSCMA.

3. Continued hasselling between physicians and Blue Cross. We are being unreasonable in some areas. They are being unreasonable in some areas. A later editorial will elaborate on some aspects of this confrontation.

4. Escalating complaints from physicians about functions of Medicaid and inability to communicate or even establish

any rapport with the S. C. Department of Social Services, which absolutely controls this program.

5. A seeming divergence in directions between SCMA and the S. C. Department of Health and Environmental Control; and the apparent paucity of physician input in its control causes us concern.

6. The apparent crisis developing in Medical Liability Insurance. It is becoming increasingly expensive and harder to get. The SCMA is studying remedies for this and there may be some hope in this area.

7. The rather ponderous and slow response of SCMA to the immediate and local needs of its members. It seems to be a problem related to and typical of any organization, despite the interest and devotion of its leaders.

8. Finally, we were disturbed by the great amount of time, effort, concern, and downright work a *few* of the members of SCMA give to our profession with little recognition and no recompense. It really is not quite fair for so few to do so much for us while most of us just sit around and complain. But that is a good subject for another editorial sometime.

Last year did not work out quite as well as I had hoped at the conclusion of the 1973 Mid Winter meeting. I overreacted then and have probably now. Things *will* be better, if we keep working.

EEK

The AMA — In Serious Condition

Most of us know by now that AMA has asked for a \$90 increase in dues for the coming year. The reasons that this is necessary were presented to the House of Delegates. Other thoughts of the AMA leadership were also presented by Hoyt

D. Gardner, M.D., member of the AMA Board of Trustees.

My own personal conclusion after this talk was that the AMA is in a serious, if not mortal, condition. The AMA has been overspending for years. It has just about exhausted its financial resources and faces bankruptcy. Even with an immediate \$90 annual per member dues increase, drastic cutbacks in AMA services will be necessary.

Some financial facts which may not be relevant or too significant were mentioned. The AMA, world's largest medical publisher, spends 16 million dollars yearly on 26 separate publications. The decision to discontinue all advertising in the JAMA was a separate and independent decision and not related to the dues increase and was not a Kennedy accommodation. The retirement fund for AMA employees has among its holdings six city blocks in the business center of Chicago, while the AMA itself is facing bankruptcy.

The AMA staff estimates that the \$90 dues increase will cause a 15 to 20% loss in membership. This estimate seems optimistic, if not self-serving. It looks quite possible that the AMA will represent a minority of physicians within this decade.

How come this moribund condition of AMA? I am not familiar with the AMA leadership, but I do know that the SCMA leaders are talented, dedicated, wise people and run an organization that is essential to our professional well-being. And we send our best and brightest (John Hawk and Harrison Peebles) to represent us at the AMA level (everybody misses Tom Parker). This makes me believe the AMA leadership is top drawer as the other state associations probably send good men (persons) to the AMA, just as we do.

Is there a message in the fact that the AMA, with good leadership, faces bankruptcy with a dwindling membership, perhaps a minority of physicians. Is it possible that a democratic organization can no longer represent the individualistic egocentric physician? Is it possible that the individual physician can stand alone and no longer needs or is able to band together to face our adversaries? Or perhaps a monolithic, union type organization would serve our purposes better?

This editorial is not intended as a requiem for the AMA but as a stimulus to consider the alternatives, *if any*.

EEK

Annotated Minutes of Meeting of SCMA Council

December 14 and 15, 1974

Francis Marion Hotel, Charleston, S. C.

Meeting called to order by Waitus O. Tanner, M. D., Chairman of Council.

Items of Business:

President's Report

1. President Don Kilgore described the Rural Health Delivery System to be presented to the House of Delegates. This was enthusiastically endorsed by Council and later by House of Delegates, and has been

greeted by the press throughout the state as an indication of care and concern for the health of the state by SCMA.

2. The President has had discussions with many people in advocacy of a Medical Examiner's System.

3. It appears that S. C. state laws are partly to blame for our medical liability insurance plight. Allowance of pre-trial

publicity and a very long (6 year) statute of limitations are examples of adverse provisions.

4. A number of problems in administration of Medicaid by the difficulty of dealing with the S. C. Department of Social Services were outlined.

5. Negotiations with Mr. Meadors seem to have reached an impasse and court action may be necessary.

Chairman of Council's Report

1. It was reported that an R.N. in Hartsville may have been providing medical treatment. This matter is being investigated and resolved by SCMA in cooperation with the S. C. Nurses' Association.

2. SCMA-SCNA have made a joint statement on the function of physician's assistants.

3. The American Academy of Family Physicians will grant credit for attendance at the Scientific Program of the 1975 Annual Meeting.

4. As most S. C. physicians have rather extensive contact with the MUSC faculty, it was felt preferable to concentrate on out-of-state speakers to make the Scientific Program more attractive.

5. Appalachian Health Council was given SCMA Council endorsement in search for M.D.s to work in the Anderson-Greenwood County area.

6. The next Mid Winter Meeting will be held in Greenville. There was considerable discussion as to the best time. The Carolina-Clemson football game sets a limit on one end, Christmas on the other. The SCMA meeting should precede the AMA meeting but not interfere with S. C. Chapter AAFP meeting. The exact time will be worked out with these considerations and will be based on hotel availability.

Treasurer's Report

1. Treasurer made a fantastic report—there is a \$13,000 surplus for 1974. This will repay only a part of the 1973 deficit,

but the financial future of SCMA appears stable.

2. Certain staff raises and Christmas presents were authorized.

3. The Treasurer recommended a mandatory activities fee for attendance at the Annual Meetings. It seems this is the practice of many organizations and is necessary for prudent management of SCMA finances. Somewhat reluctantly, Council passed this and presented it to the House of Delegates, where it later passed.

4. Because of federal income tax regulations, SCMA may have to establish profit making and charitable organization subdivisions to ensure deductibility of some of our functions. Staff is studying this for future recommendations and action.

Staff Report—Charles Johnson

1. Ron Harris has been added to the SCMA staff as Director of Legislative and Public Relations. His positive input has already been felt.

2. There are 1207 licensed physicians in S. C. who are not members of SCMA. We must recruit these physicians for SCMA.

3. S. C. Health Policy and Planning Council wants to control physician profile statistics for their Health Manpower Program. It will pay SCMA 50¢ per physician if SCMA will collect and store this information. It will cost SCMA about \$2.50 per physician to do this, but it appears preferable for SCMA to be the repository of this information, even at a loss, than to give HP&P Council full possession of this information.

Councilors Report

Councilor from the Fifth District reported attendance at a meeting of the Medical Advisory Board to S.C. Department of Health and Environmental Control on December 12, 1974. Only 4 of the 12 on the Medical Advisory Board were practicing physicians. The Board recom-

mended either increasing State Narcotics Licenses from \$5.00 per year to \$50.00 per year or selling prescription blanks in numbered triplicate sets which must be used for narcotic Rx's with a file kept.

2. Councilors reported many problems with Blue Cross-Blue Shield, and especially Medicaid. Relationship between BC-BS and S. C. Medical Care Foundation are somewhat strained.

3. A meeting with the Governor-Elect was reported to portend better relationships but increased responsibility on SCMA.

At this point, Council was adjourned for an executive meeting between President of BC-BS and a selective, elite group of Councilors.

Council reconvened at 7:30 a.m. on Sunday, December 15, by Chairman Tanner.

Some resentment that some Councilors were excluded from the meeting with BC-BS President was expressed.

A suggestion that Council meet monthly was discussed but it was decided to continue having Council meet on alternate months and the Executive Committee meet on the intervening months. Of course, Council is always on call for urgent business.

Council heard Dr. Don Brake of Conway present his views on retroactive denials of hospital admissions. The Council was in sympathy with Dr. Brake's position but took no effective action.

Council was then adjourned to attend House of Delegates meeting.

EEK

The Pain Phone

When a telephone prescription for pain relief is necessary or convenient, you can call in your order for Empirin Compound with Codeine in 45 of the 50 states† That includes No. 4, which provides a full grain of codeine for more intense, acute pain.

†The exceptions: Alaska, Arizona, Maine, Oregon, Rhode Island, and the District of Columbia

**EMPIRIN[®]
COMPOUND
& CODEINE**

No. 4 codeine phosphate*
(64.8 mg) gr 1

No. 3 codeine phosphate*
(32.4 mg) gr 1/2

Each tablet also contains aspirin
gr 3 1/2, phenacetin gr 2 1/2,
caffeine gr 1/2.

*Warning - may be habit-forming

YOU'RE ALWAYS WELCOME
at our
headquarters
in
Research Triangle Park
North Carolina.

CALL OR WRITE FOR
FURTHER
INFORMATION

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Changes in the Mental Health Law

Please take note that on January 5, 1975, recently passed amendments to the present Mental Health law pertaining to the admission procedures for the mentally ill will go into effect. These amendments will necessitate a somewhat altered role of the physician in the commitment procedures. All involuntary commitments of individuals for indefinite terms will require judicial hearings. The individual alleged to be mentally ill must be examined by two designated examiners appointed by the Probate Court. One of these designated examiners must be a licensed physician; the other may be a person designated as specifically qualified by the Department of Mental Health. If the examiners conclude that the individual is mentally ill and in need of care and treatment in a hospital, a hearing will take place thereafter in the Probate Court, and the examiners will be expected to personally testify at this hearing as to their findings, and face cross-examination—a major change in the role physicians have played in the past.

In addition, on January 5, 1975, the State Hospitals will no longer accept patients on existing admission forms. The new forms will be available at the Probate Court of each county, after January 1. Conditionally discharged patients on January 5 will no longer be involuntarily readmitted to the hospital, except on proper Order from the Probate Court.

For information on this Act, contact the Office of the Attorney General, Judicial Commitment Section, P. O. Box 11549, Columbia, South Carolina 29211. Telephone: 758-3970.

PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies* Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

ROERIG **Pfizer**

A division of Pfizer Pharmaceuticals
New York, New York 10017

**Pinworms, roundworms controlled
with a single, non-staining dose of
ANTIMINTH[®]
(pyrantel pamoate)**

equivalent to 50 mg. pyrantel/ml.
ORAL SUSPENSION

*Data on file at Roerig.

Please see prescribing information on facing page.

ANNOUNCEMENTS

Dr. William H. Prioleau, Jr., of Charleston has recently limited his practice to thoracic and cardiovascular surgery.

Direct Relief Doctor—Aesculapian International sends volunteer physicians and other professionals to medically deprived areas. 130 assignments were made last year, including the U.S., Latin America and Caribbean, Far East, South Asia, and Africa.

The physicians do clinical work, teach or temporarily replace local doctors, and, in most, cases, take their families along. Room and board and transportation are usually provided, plus compensation based on the local economy.

Interested physicians should write to Direct Relief Doctor, Aesculapian International, P. O. Box 1319, Santa Barbara CA 93102.

Sixth Annual Family Refresher Course presented by the Division of Continuing Education at MUSC will be held February 9-15, 1975, in the Heyward-Lynch Room of the Mills Hyatt House Hotel in Charleston, S. C.

Registration fee: \$140. To be presented are reviews of the recent advances in internal medicine, surgery, pediatrics, neurology, psychiatry, ob/gyn, otolaryngology, orthopedics, and family practice.

Write to: Director, Division of Continuing Education, Medical University of South Carolina, 80 Barre Street, Charleston SC 29401.

S. C. Society of Medical Technology and S. C. Department of Health and Environmental Control will present "Medical Mycology, 1975," February 27 and 28, 1975, in Columbia.

For further information, contact Ms. Susan Cheatham, Laboratory Improvement Section, S. C. Department of Health and Environmental Control, 2600 Bull Street, Columbia SC 29201, telephone (803) 758-5464.

Rondomycin[®]

(methacycline HCl)

CONTRAINDICATIONS:

Hypersensitivity to any of the tetracyclines
WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**

Usage in pregnancy. (See above **WARNINGS** about use during tooth development.) Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate observed in premature infants given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines. To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days. Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms) anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia. Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea. In uncomplicated gonorrhea, when penicillin is contraindicated, 'Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule: 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of 'Rondomycin' (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia: 900 mg daily for six days.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses. Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.
SUPPLIED: 'Rondomycin' (methacycline HCl): 150 mg and 300 mg capsules, syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev 6/73



WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512



When the focus is on bronchitis due to susceptible strains of *H. influenzae* and pneumococci*

Rondomycin[®] 300_{mg.}
[methacycline HCl] Capsules

Delivers from the very first dose:

Studies show that after the first dose serum levels rapidly rise above minimum *in vitro* inhibitory concentrations

*Since many strains are known to be resistant, routine sensitivity testing is recommended.

The Role of the Detail Man

"I may be prejudiced, but I am very much in favor of the detail men I meet. Most of them are knowledgeable about the drugs they promote and can be a great help in acquainting me with new medication."

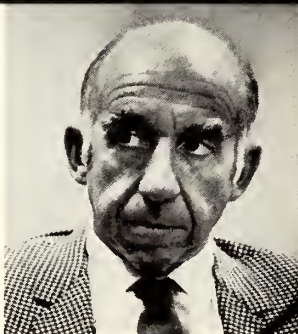
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.

Dr. Willard Gobbell
Family Physician
Encino, California



Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School



"In the total picture of dealing with health problems in this country there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be — and at times actually are — disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets — some of it scientifically sound and therefore truly useful — as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. I go without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard they are ambitious and improperly motivated. A sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and determined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—i.e., the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

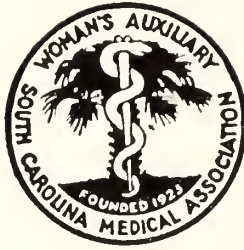
tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

*Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005*





WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION

"How Do You Relate To Medical Auxiliary?"

The concept for auxiliary is that it should be the "first club" for all wives of physicians because of the tremendous value it can be, (1) for public relations for the physicians and their wives and (2) service to the community. The "first club" is a resource center for all other civic and service clubs and organizations.

According to a recent survey of some state auxiliaries, these are a few reasons given for becoming affiliated with the medical auxiliary: (1) Interest in husbands profession; (2) Belief in the principles for which the auxiliary stands and the corresponding beliefs of the medical profession; (3) Opportunity to aid and work with physicians and their medical societies out of a loyalty to medicine; (4) Pride in being a physician's wife and wishing to identify with a group of physicians' wives who have the same interest, responsibilities and problems; (5) Opportunity to communicate concerns about health care to the community; (6) Concern over the vitality and essence of life itself; (7) Interest in increasing knowledge, in legislative and other areas.

Do you relate to any of these reasons given? You can become an active part in working with auxiliary members with the same interest and ideals. Or, are you one who is afraid to get involved and willing to sit back and let someone else carry the banner on behalf of medicine? Maybe this is why the profession is not looked upon

in as friendly relations as it once was. Why is it society points its finger to the medical family and insists that we are more interested in material possessions than we are in the medical care of our communities? Have we been negligent in demonstrating to the public that we do care and are working to help solve health problems in our communities and state?

We need to be well informed about legislative issues concerning medicine. Because you have more time to give to this project than your physician-husband, you can be of great help. And who else should be more concerned about medical legislation than you the doctor's wife? Work to preserve the physician-patient relationship—dear to the patient and necessary for the physician in order to practice medicine in a free and independent manner. Each year more and more laws are being written at both the national and state levels that concern health, health care, and the delivery of health care. If we don't take an interest now, laws will be passed that may not have the physicians' and patients' best interest in mind.

More students than ever before are resorting to AMA-ERF'S "Loan of last Resort," according to Mrs. C. M. Lessenden, Jr., national AMA-ERF chairman. Because of a decrease in federal grants and fewer subsidized interest loans, medical students without collateral are turning to the Student Loan Guarantee Program where the AMA acts as co-signer on the student's note. Greater use of the loan

program makes it increasingly important for physicians and their wives to support the AMA-ERF program. "Remember", she says, "giving through AMA-ERF is an investment in medicine's future." Members-at-large may send their contributions made out to AMA-ERF to Mrs. Andrew J. Whitaker, 6106 Crabtree Road, Columbia, S. C. 29206.

Our goals have been set high this year (they were outlined in the September issue of the Journal), and we are striving to reach them. As the result of the South Carolina Forum on Child Protection held last March with the assistance of the Medical Association, the Auxiliary is fulfilling its obligation to take the program to the county level. At this time, those that I am aware of, multi-disciplinary committees have been organized in Charleston, Greenville, Spartanburg, and York counties. Newberry county has conducted a program on child protection with great news coverage. York county held a county Child Protection Forum with 257 persons attending. Spartanburg county plans a forum in January which will include several surrounding counties.

October 31 and November 1 the state auxiliary sponsored a very successful Health Careers Rally in Charleston with approximately 3,000 students from all over the state attending.

Many county auxiliaries were involved with the Hypertension Screening being conducted in the state in November and some auxiliaries have joined other agencies in conducting free pap smear clinics. Many of our county auxiliaries are involved with eye screening tests in the public schools, sponsor Health Careers Clubs and collect drugs and make hospital coats and bandages for International



Mrs. Wayne C. Brady

Health.

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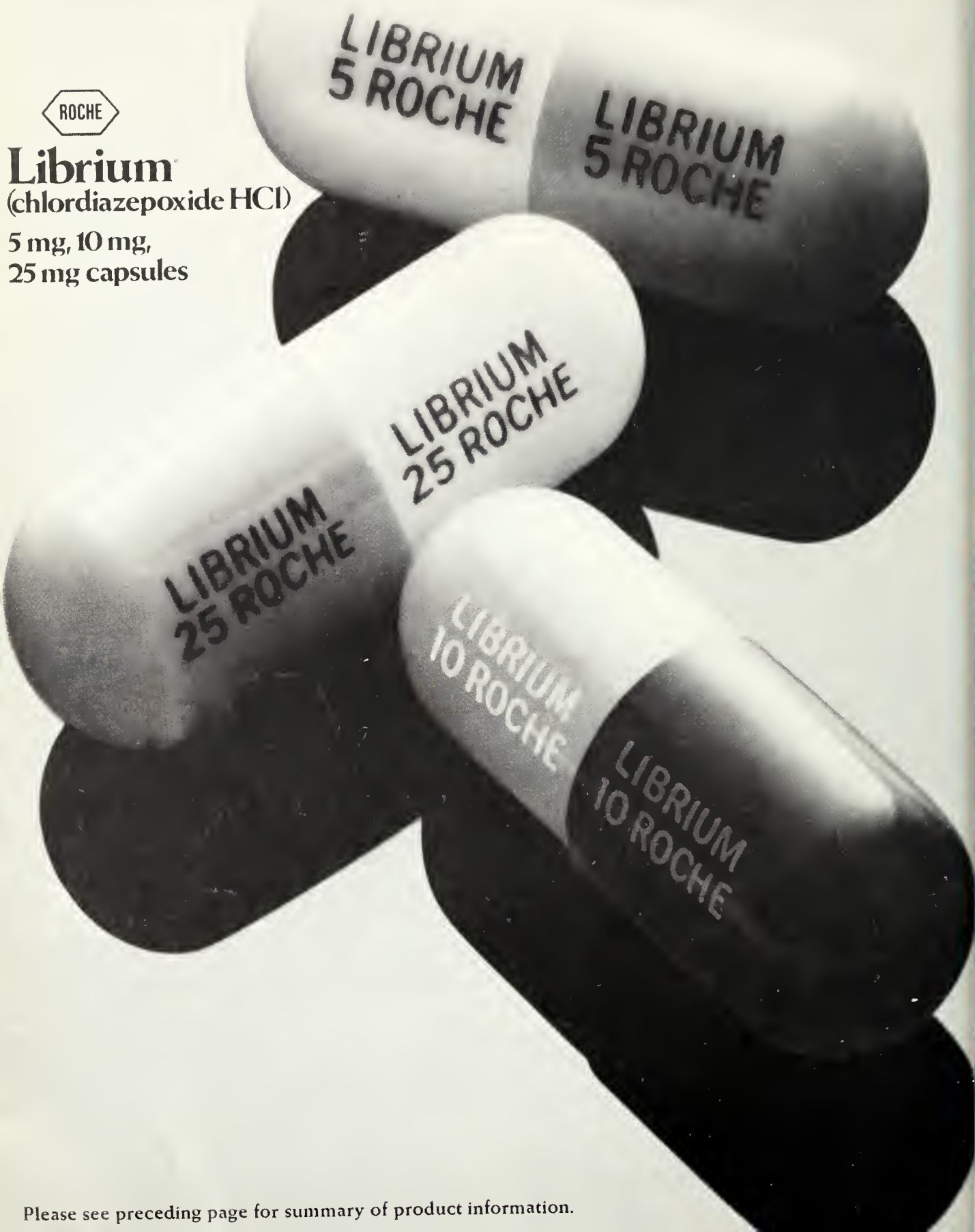
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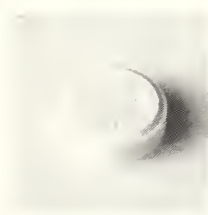
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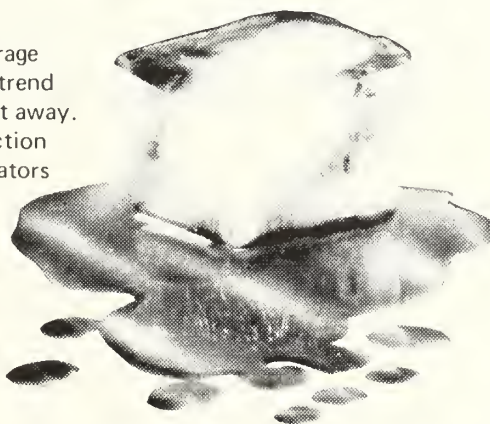
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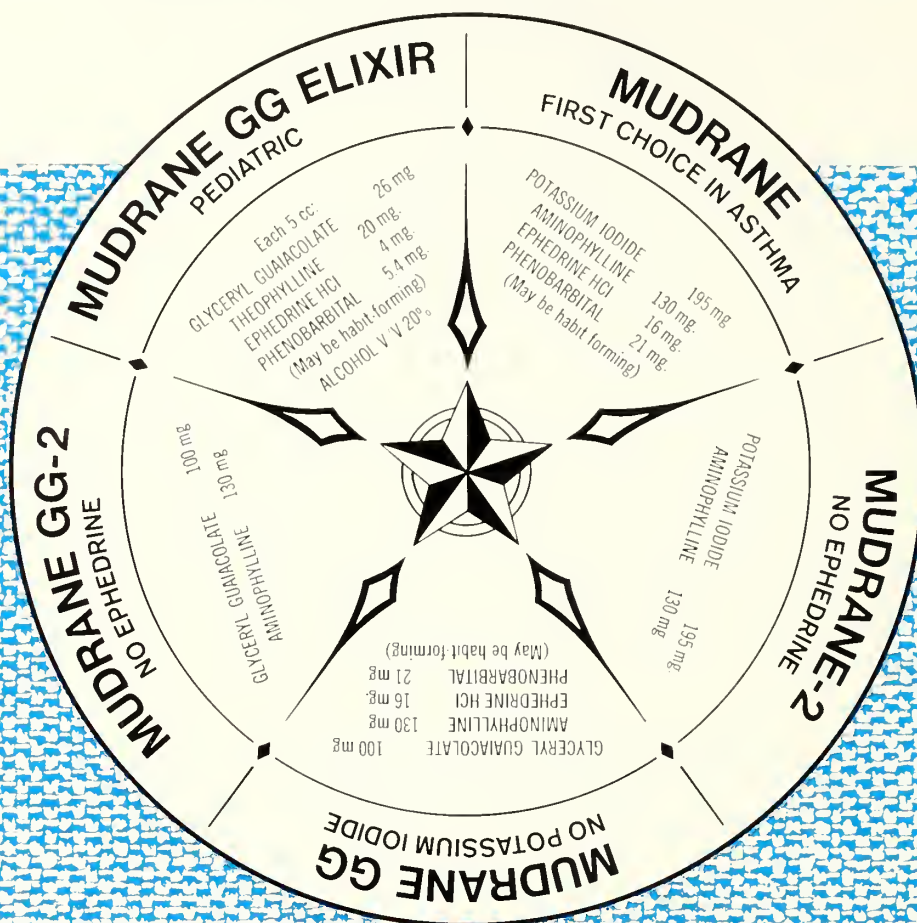
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SOUTH CAROLINA MEDICAL ASSOCIATION

VOLUME 71

FEBRUARY, 1975

NUMBER 2

THE OFFICE MANAGEMENT OF HYPERTENSION

FREDERICK E. NIGELS, M. D.*

The clinical practice of medicine today offers few situations in which prevention of premature disease and death is so clearly possible as in the treatment of hypertension. The recognition of hypertension as the major health hazard of our adult population has resulted in a somewhat belated but now massive attack on this disorder by some 30 health agencies in this country. One of the results of this approach will be to present enormous challenges to our health care system, especially practicing physicians. Problems related to methods of case-finding, volume load of new patients, education of patients, and continuing professional educational will have to be faced. Solutions will require the commitment that physicians would give to any other epidemic which affects a significant part of their practice.

The past 25 years have brought dramatic changes in our approach to hypertension. Epidemiological studies have been crucial to our current understanding of the enormity of the problem in this country—the tremendous number of patients involved and the devastating consequences of untreated hypertension. Large scale

studies over the past 10 years have established the fact that 20-30 million people in this country have hypertension, only half of whom are aware of having this disease, now recognized as the leading cause of strokes, congestive heart failure, kidney failure and a major risk factor in coronary artery disease. Sadly, only one eighth of hypertensive patients are currently receiving adequate therapy.

As a result of the information from the Framingham study, the VA Cooperative Studies and others, there can be little argument as to the value of antihypertensive therapy in any patient with moderate to severe hypertension and in most patients with mild hypertension. Fortunately, during this period of rapidly expanding information, effective drugs have become available so that we now have a truly effective armamentarium of agents capable of lessening future vascular catastrophes for a great many people.

This is not to imply that all the answers are in, by any means. In fact, we are probably in a comparatively primitive era in relation to this disease. Many questions remain to be answered and new areas of needed investigation are continually opening. Despite the remarkable advances in therapy over the past 25 years, we are

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still operating in a primarily empirical manner. With recent advent of new knowledge involving the renin-angiotensin-aldosterone system, for instance, we appear to be at the brink of exciting new directions which will allow treatment to be planned on the basis of the major pressor mechanisms involved in an individual case. We look forward to simple, inexpensive, non-invasive techniques for determination of cardiac output and blood volume, readily available measurements for plasma renin activity, angiotensin and aldosterone, etc. New drugs and techniques are, of course, under study constantly. In the meantime, we must still live with empirical therapy which is, fortunately, remarkably effective in most cases.

WHO NEEDS TREATMENT

As mentioned above, there can no longer be any valid argument against treating all hypertensive patients with sustained diastolic pressures above 104 mm Hg. For patients with diastolic pressures between 90 and 104, and those with systolic elevations alone, other factors should be considered as one contemplates diagnostic and therapeutic programs. The presence of other risk factors such as diabetes and hypercholesterolemia and family history of premature vascular disease would weigh heavily in favor of treatment. Age is certainly important in deciding upon the necessity of extensive workup as well as in planning therapy: the younger the patient the greater the need for an intensive approach in both spheres. Blacks do not tolerate hypertension as well as Caucasians nor males as well as females, facts which will also influence one's decision. The presence of target organ damage makes therapy almost mandatory in mild cases and may indicate emergency therapy in cases with diastolic above 125 mm. Systolic pressure elevation, with or without diastolic hypertension, is not to be ignored. In fact, the Framingham study has shown systolic pressure elevation to be a major factor

for stroke and other vascular complications.

EVALUATION

A single blood pressure reading does not furnish adequate data upon which to base judgments regarding work-up and therapy. Cases of accelerated (malignant) hypertension and certain severe complications require immediate hospitalization and therapy, of course, but other patients should have three determinations on different days, in fairly relaxed surroundings, and preferably should have home readings included. (Later, during the course of therapy, home readings are also helpful in evaluating therapy, in maintaining patient adherence to drug schedules, and in decreasing the number of office visits.) Be sure to exclude oral contraceptives as a causative factor.

A diagnosis of hypertension having been established, one can, with a minimum of difficulty and expense, evaluate the target organs for hypertensive damage, screen in a preliminary manner for curable causes of hypertension, and obtain baseline studies on those factors that may be influenced by therapeutic agents. A reasonably complete history and physical examination with PA chest film and EKG will reveal signs of left ventricular hypertrophy, congestive heart failure, cerebral damage, retinal involvement, and most significant peripheral atherosclerosis. Coarctation of the aorta will be detected by examination of the force and timing of the femoral pulse. The history will reveal suggestive symptoms in almost all cases of pheochromocytoma — paroxysms of hypertension with headaches, tachycardia, palpitation, and often with weight loss and tremors suggesting hyper-metabolism. Cushing's syndrome will almost always present other physical evidence than hypertension alone: characteristic body habitus and skin changes, hyperglycemia, etc.

Basic laboratory studies should include CBC, blood sugar and cholesterol to assist in uncovering other major risk factors.

Serum creatinine and careful urinalysis will reveal most significant cases of renal failure (but not renovascular disease). A serum potassium is certainly indicated prior to beginning therapy. A low value with the patient on a normal diet and without prior thiazide therapy indicates the need for further study of the renin-aldosterone metabolism. It seems highly likely that, in the near future, properly performed determinations of plasma renin activity will become a recommended procedure. Uric acid level should be known before initiating thiazide therapy.

Until fairly recently, the best medical principles indicated a vigorous search for surgically curable cases but it is now obvious that certain compromises must be made. A complete work-up employing the currently available techniques can be an extremely expensive, moderately dangerous procedure and obviously cannot be made available to but a small percentage of the hypertensive population. Fortunately (or unfortunately) only about 10 per cent of patients will be found to have secondary hypertension, and only about half of these will be correctable, mostly reno-vascular cases. This latter cause may be suspected in cases of sudden or recent onset of hypertension, abrupt worsening of hypertension, onset before 35 years of age, failure to respond to treatment, and/or the presence of a to-and-fro bruit in the upper abdomen. Such situations warrant thorough studies such as rapid sequence I.V.P.'s, renal angiography, etc. Similarly, studies for pheochromocytoma, primary aldosteronism, Cushing's disease, and more elaborate renal function studies are also indicated only in cases where suspicion has been directed to specific diagnosis by findings or events mentioned above.

DRUG THERAPY

No attempt will be made to review all the drugs in current usage. The PDR is said to contain some hundred or so preparations for hypertension. For the office treatment of most patients, however, the

list of drugs with which one needs to become familiar is not extensive. These drugs can be classified as diuretics, vasodilators, and sympathetic blocking agents. Drugs should be introduced singly until pressure is controlled, but when several drugs are required, it is sometimes possible to attain a combination which can be given in one tablet, thereby improving patient cooperation. Lifelong therapy must be expected, and so should be simplified where possible.

The program should begin with a diuretic. The thiazides and chlorthalidone are most effective here. Furosemide (Lasix®) and ethacrinic acid (Edecrin®), though most potent diuretics, are less effective hypotensive agents and should be reserved for patients with renal failure or patients who will not respond to other diuretics. A thiazide such as hydrochlorthiazide 25-5 mg. once a day, increasing to 50 mg. b.i.d. if necessary, or chlorthalidone (Hygroton®) 50 to 100 mg. once a day make the best and least expensive basic program. The latter diuretic has some advantage by virtue of its longer effect and therefore once-a-day dosage. Adverse side effects are rare but may include purpura, pancreatitis, rash, GI distress, elevated urea and uric acid, gout, increased glucose, and decreased potassium. Asymptomatic hypokalemia need not be treated in most cases, but should be avoided in patients on digitalis and with myocardial irritability, as in recent infarction. If therapy is indicated, the combination of a thiazide with a potassium-sparing agent (Aldactazide® or Dyazide®) should be substituted, rather than attempting potassium supplements.

If the diuretic is not sufficient to attain normal B.P. in 2-3 weeks, then the next level of therapy should be added, continuing the diuretic. Some physicians utilize rauwolfia derivatives such as reserpine 0.25 mg. once or twice a day. Depression, diarrhea, nightmares, nasal congestion and increased gastric acidity are frequent results if adequate dosages are employed,

seriously limiting the usefulness of these drugs.

Hydralazine makes a good second (or third) choice, to add to the thiazide. This drug is a vasodilator and may cause troublesome headaches. Starting treatment with 25 mg. b.i.d. and restricting dosage to a maximum of 50 mg. t.i.d. will usually avoid the lupus-like syndrome associated with high dosage. It results in sympathetic stimulation with tachycardia and increased cardiac work, possibly dangerous for patient with coronary disease or myocardial failure. Propanalol (Inderal®) may be added in selected patients to block this cardiac effect.

Inderal, the only beta-adrenergic blocking agent available in this country, has not yet been approved by the FDA for use in hypertension. However, this drug suppresses renin release by the kidney and can control many cases with high renin levels. It is contra-indicated by congestive heart failure and asthma but otherwise may be a very effective "second" drug.

Methyldopa (Aldomet®) is also an effective agent at this level. Its mechanisms of action are unclear but include a probable central nervous system effect on peripheral vascular tone and depression of renin activity. It may cause drowsiness and lassitude, fever, and anemia. It should always be used with a diuretic because of its tendency to cause fluid retention. One begins with 250 mg. two or three times a day and may increase up to 2 gm. a day.

Should the above combinations still prove insufficient, then guanethidine (Ismelin®) should be added. This drug, a powerful sympathoplegic agent, exerts its most dramatic effect in the form of orthostatic and exercise hypotension. Starting doses of 10 mg. daily may be slowly increased to 400 mg. In addition to postural hypotension, retrograde ejaculation and diarrhea may seriously limit its acceptance by the patient.

When one is faced with severe (but not malignant) hypertension, diastolic pres-

sure above 120 mm, therapy may be initiated with two drugs. With diastolic above 140 mm, three drugs may be utilized.

Certain complications may dictate a specific approach to drug therapy. In CHF, for instance, propanalol is contra-indicated, and the tendency to fluid retention limits the use of hydralazine and reserpine. In azotemia, the thiazides and guanethidine are relatively contra-indicated, with furosemide, methyldopa, hydralazine and propanalol being preferred. In coronary artery disease, oral diuretics, methyldopa and propanalol are well tolerated—others less well, especially hydralazine unless combined with propanalol. In cerebral artery insufficiency, drugs with marked postural effect should be avoided: guanethidine, pargyline, etc. Hypertensive therapy should be withheld for 4-6 weeks after myocardial or cerebral infarction, unless hypertension is severe.

GENERAL CONTROL MEASURES

Diet: Obesity should be corrected where possible, but weight loss is unlikely to create a significant fall in blood pressure. Advanced azotemia may require limitation of protein. Diabetes and hyperlipidemia should be treated appropriately. Salt restriction, long a talisman in blood pressure control, has not been found effective unless carried to almost intolerable degrees (less than 200 mg. per day). The incorporation of diuretics in the regime of therapy now allows a patient to use 2-5 gm. a day. Large sodium intakes (above 10 gm. a day) can prevent the antihypertensive effect of the usual diuretic dosages and should therefore be avoided.

Rest, exercise, etc.: Although cardiac and other complications may require certain adjustments, hypertension alone rarely necessitates specific changes from a normal healthful life style. Advice to "slow down," change jobs or work schedules, etc., is unlikely to be effective or even heeded. Isometric exercises should be avoided.

Tobacco and alcohol: Cigarette smoking

is also a major risk factor in coronary artery disease and should be avoided, although its effect on blood pressure is variable. Excessive alcohol intake may elevate blood pressure.

MALIGNANT HYPERTENSION

Malignant (or accelerated) hypertension will not be discussed here. This syndrome as well as other hypertensive crises (hypertensive encephalopathy, pheochromocytoma, eclampsia, dissecting aneurysm, etc.) are medical emergencies requiring hospitalization and immediate lowering of blood pressure, usually with parenteral drugs beyond the scope of this article. Once the initial crisis has been controlled, the long term treatment of the hypertension is often surprisingly simple, with the oral agents described above.

COMMENT

It has become obvious that hypertension is one of our major health problems, from the standpoint of prevalence, morbidity and mortality; that it can be readily detected; and that effective drug therapy

is available. The disturbing statistics in regard to the huge numbers of undetected and untreated cases indicate the need for thoughtful new approaches to detection, especially through presently available medical facilities. All physicians must be urged to measure B. P. in any patient contact; B. P. readings should be routine in all dentists offices; all emergency room cases should be checked. B. P. readings can be made available at all blood donor centers, pharmacies, industrial health facilities, etc. Mass public screening is undergoing extensive trial.

But case finding is of no value (and could be harmful) unless adequate sources of medical care and follow-up are available. Such care will not be available unless all primary physicians are convinced of the necessity for proper study and treatment of the hypertensive at all stages, are cognizant of available drug programs, and stay abreast of the rapidly expanding advances in this critical field.

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PREDICTION OF POSTCARDIOTOMY PSYCHOSIS

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Attention given to behavioral disturbances in postoperative heart patients in multiple studies utilizing psychological, organic, or combined approaches has provided as many questions as answers. Lee,¹ and other authors²⁻⁷ have clearly defined the following organic factors: duration of perfusion time, operative hypotension, implantation of valve prostheses, and the presence of long standing organic heart disease (symptoms five years or longer). On the other hand, psychological studies of factors involved, although helpful in the total care of the patient, have been less precise in identifying the patient at risk for postoperative psychosis and those psychological factors necessary for an uneventful postoperative recovery without significant behavioral complications. The objective of this study is an attempt to predict preoperatively those patients who will experience a postoperative psychosis and, if possible, identify the significant factors based on an ego psychology approach.

METHODOLOGY

Twenty-five consecutive patients admitted for cardiac surgery to the Thoracic Surgery Service of the Medical University of South Carolina Teaching Hospital were examined preoperatively. Informed consent was obtained after the nature of the procedure was explained. The patients were administered the Tapping Test, Form Board Test, Object Assembly Test (from Wechsler Adult Intelligence Scale), Peabody I.Q., Pursuit Rotor Test, Trail Making Test, and The Minnesota

Perceptuo-Diagnostic Test to determine presence or absence of brain dysfunction. The psychiatric interview was initially an open ended approach but contained 24 questions (Table I) which enabled the examiner to rate the patient's preparedness for the forthcoming surgical experience. During the interview attention was specifically addressed to the patient's previous and present coping patterns, expectations of surgery, past medical history, affect, ego defenses, and a mental status examination. The preoperative psychodynamics were formulated in terms of regressive alterations of ego functioning, object relationships and identification processes. As a result of the interview, the patient's overall preparedness was then rated on a 1 to 5 scale in the following categories: repression, denial, object relations, and depression. Using this information, an overall score of 1 to 5 was assigned to each subject. It was expected that four subjects would experience a postoperative psychosis (Table II), based on a preoperative score of 3 or more.

Following surgery the patient was evaluated on each of the first seven consecutive postoperative days for level of ego functioning, cognitive processes, and anecdotal material including dreams. On the basis of these interviews each patient was assigned a postoperative rating from 1 to 5 according to the behavior exhibited. For the duration of the patient's hospital stay, behavioral ratings were made on each patient daily by the nursing staff by the following criteria: sleep, agitation, delusions, hallucinations, and mood. These behavioral manifestations were correlated

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TABLE I

INTERVIEW FORMAT

1. What type of person are you?
2. What kind of person do you think you are?
3. How easy is it for you to trust others?
4. Do you have many friends?
5. Are you a loner? Past or present?
6. How would you describe your relationships to persons of the opposite sex? Past and present?
7. How would you describe your mother as a person?
8. How would you describe your father as a person?
9. How close were you to your mother in your early life? Father?
10. What type of person do you think others think you are?
11. Is there one thing in your life you wish you could go back and change?
12. Do you feel that you have been unfair to yourself or anyone else in your life?
13. What things in life frighten you the most?
14. In which part of the body do you think a man's soul is?
15. Wonder why people sometimes attribute feelings to a person's heart?
16. What is your idea of what surgery will do to your heart?
17. As you see it, how will the operation on your heart affect you?
18. Have you been seen by the person who will put you to sleep?
19. How do you feel about undergoing anesthesia?
20. What concerns you the most about the surgery you are about to have?
21. Occupation: past — present
22. Present family life: brief history children
23. How would you describe your spouse as a person?
24. Have you ever been bothered by nightmares?
25. Do you have difficulty sleeping now or in the past?
26. Have you ever had fainting or dizzy spells?
27. Have you ever felt like you were not the same person after a traumatic event in your life?
28. Have you ever had — ulcers, hypertension, stress diarrhea, ulcerative colitis, chronic back pain, headaches (migraines)?
29. What do they plan to do to your heart?
30. Has there been any change in your religious life lately or your relationship with God?

TABLE II

PSYCHOPHYSIOLOGICAL RATING
SCALE OF POSTOPERATIVE
REACTIONS

1. Anesthetic/analgesic effects only
2. Delusions but self-corrected or external source
- Anxiety intermittent
- 24 hours after surgery able to relate details of surgery performed
3. Delusions
- Illusions
- Depersonalization
- Sustained anxiety
- 24 hours after surgery unable to relate details of surgery performed and if able to do so only with intense anxiety
4. Hallucinations
- Delusions
- Illusions
5. Dementia with organic involvement

so that a nurse's rating of three would correspond to the psychiatrist's rating of three in severity of disturbance.

RESULTS

A rating of 3 was chosen as the pivot number because the behavior described was consistent with postoperative psychosis. The four patients assigned a rating of 3 or greater preoperatively were given postoperative ratings of 3 or more by the nurses as well as the psychiatrist. Seventeen subjects obtained a rating of 2 or less preoperatively while postoperatively 16 of the 17 obtained a rating of 2 or less. Four of this group of 25 subjects died postoperatively within the first 48 hours. Thus, with the exception of one patient, the grouping (based on psychotic versus nonpsychotic behavior) chosen by the psychiatric examiner preoperatively corresponded with the groupings obtained by the nurses who rated the patients postoperatively. The occurrence of such an event by pure chance would be $<.001$.

The correlation between nurse's rating in the various categories ranged from .59 to .65 with a median of .61. This would suggest that substantial correspondence among the nursing staff in their ratings did exist. Since earlier studies^{1,2} pointed to a predominance of behavioral manifestations in the first 72 hours postoperatively, a comparison of the nurse's rating scores was undertaken to compare the validity of these earlier studies. Using the McNemar Test for the significance of change, analysis of the behavior ratings confirmed that most psychological reactions occurred during the first 72 hours. ($X^2=10.00$ $DF=1$, $p <.001$). To rule out hallucinatory side effects of medications, a drug survey was conducted. One patient received Talwin (100 mgs. daily for three days) but no evidence of hallucinations was found in that individual.

Lastly, there was no correlation between the results of the preoperative tests for organic brain dysfunction and the psychotic behavior observed postoperatively.

DISCUSSION

How does this approach differ or compare to earlier ones? Meyer⁸ and Fox⁹ described severe postoperative disturbances after mitral operation and established some insight into this phenomenon as a multivariable syndrome. Over the next decade many possible etiological factors were explored. Kornfeld⁷ focused on double valve operations, length of stay on the pump oxygenator, preoperative brain damage and the ICU environment thus expanding the hemodynamic, metabolic, and environment etiological determinants. Hazan⁵ investigated silicone fluid emboli, fat embolization, decreased liver metabolic activity, and the release of abnormal circulating amines from damaged heart muscle thus expanding the hemodynamic and metabolic determinants as a function of extracorporeal circulation. The expansion of these determinants, metabolic and hemodynamic, continued with Lee¹ focusing on a microvascular perfusion defect generated by extracorporeal circulation. Blachly⁶ found elevated urinary catecholamines and lowered cardiac output with resulting cerebral anoxia and Gilman⁷ described focal embolic lesions of the dominant parietal lobe. At the same time others were examining the psychic and environmental determinants. Abram¹⁰ focused upon the symbolic threat to life and the inherent defense mechanisms used. He also investigated the importance of the ICU as a variable stress factor. A shift began in the late 60's expanding the psychic determinant. Dlin¹¹ describes the "six dynamic phases" of impaired ego defenses. Kimball¹² alluded to higher mortality among patients manifesting preoperative anxiety or depression and also found a higher psychological morbidity among cardiectomy patients. Lazarus,¹³ in a controlled study, found the psychiatric relationship helpful in decreasing postsurgical psychological reactions. He further saw the postsurgical psychosis as "a state of ego disorganization—a final common pathway for the ex-

pression of psychological, environmental, and organic factors."

Insult to the CNS in postcardiotomy phenomena should be viewed as an insult to the entire psychic apparatus. Because of different morphological determinants, certain neuronal groups and areas will have varied and at times complex responses to specific derangements with resultant clinical manifestations. These manifestations will vary in quality in direct proportion to the etiological determinant (psychic, metabolic, hemodynamic, and environmental) such that each may manifest independently or in multiple combinations. The consideration of psychic processes as having a separate and independent expression as well as having an expression closely related and interrelated to metabolic, hemodynamic, and environmental determinants does not contradict or refute the current hypotheses about CNS derangements. Rather, it adds new dimensions. It allows for separate independently functioning subsets which are contained in a part of the whole but whose independent expression will alter greatly the interreaction and the range of responsiveness and action of the whole system.

Evaluation of cardiectomy patients preoperatively by means of an ego psychology approach revealed that it was a valid

predictive indicator of postoperative behavioral manifestations. This study, utilizing predictive factors of repression, object relations, denial, and depression in relation to psychotic versus nonpsychotic behavior, correctly predicted the reactions of 20 of 21 patients.

Behavioral manifestations observed preoperatively and postoperatively revealed that 16 of 21 patients in this study had no observed psychotic behavior during the course of their hospital stay. It is felt from these observations and interactions with the patients that a significant number of patients do not experience psychotic phenomena as a result of cardiectomy at least during their hospital stay. It would seem likely that such patients are protected by repression which appears to have been operating poorly in those patients who exhibited psychosis.

The results of this study emphasize the importance of considering psychic functioning as an independent but interrelated force in the determination of postcardiotomy behavioral phenomena. This study also concludes that the independent force of psychic functioning may well be the most important factor in predicting postcardiotomy psychotic phenomena. Indeed, this study suggests that an ego psychology approach in postcardiotomy patients is valid.

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A NEW METHOD FOR CORRECTION OF CONGENITAL INTRACARDIAC DEFECTS IN INFANCY OR BACK TO THE ICE-AGE

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Even though tremendous advances have been achieved in cardiac surgery during the last two decades, the correction of intracardiac defects in infancy has remained a disappointment in many centers until recently. In the past, medical management and palliative extracardiac procedures have been the cornerstones of therapy until some ideal age and weight were attained. At that time, total correction of the defect using conventional extracorporeal circulation would be performed. Unfortunately, a significant number of infants die from complications before attaining the ideal age and weight. For example, many infants with transposition of the great vessels die from cerebrovascular accidents or become inoperable because they develop pulmonary vascular hypertension.

An alternative to medical management or staged palliation and repair in high risk infants has been early correction using extracorporeal circulation. However, the mortality has been as high as 70 per cent using this approach due to technical difficulty and pulmonary, renal, and metabolic complications.

Faced with (1) the failure of medical therapy and palliative procedures for some infants with defects such as transposition of the great vessels, Tetralogy of Fallot, and ventricular septal defects,

(2) the high mortality of conventional extracorporeal circulation, and (3) the absence of palliative procedures for defects such as total anomalous venous return, we have recently turned to the technique of surface-induced profound hypothermia with limited extracorporeal circulation and circulatory arrest. This technique was developed in 1964 by Hisaka¹ in Japan and popularized since 1969 by Barratt-Boyes² in New Zealand.

The technique of circulatory arrest has distinct advantages over extracorporeal circulation. They are a totally bloodless, still operative field uncluttered by vascular cannulas (which enables an accurate and rapid repair of the cardiac defect), and a reduction in total bypass time (which reduces the incidence of complications).

A major concern has been whether the circulation can be stopped long enough for the repair to be corrected. From the work of Gordon, et al in 1960 (See Table I),³ one can readily appreciate that as temperature is reduced oxygen consumption is likewise reduced, provided that the patient is prevented from increasing his oxygen consumption by shivering (in the older patient) or non-shivering thermogenesis (in the newborn). According to Gordon's data, the circulation can be safely arrested at 16 C for 32 to 40 minutes. In actual clinical practice many investigators have found that circulatory arrest can be performed safely at 20 C for as long as 60 minutes.^{2,4,5} This is long enough for most defects to be corrected by

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TABLE I^a

Theoretical Oxygen Consumption and
Safe Period for Total Circulatory
Occlusion at Different Body Temperatures

Temp.	Oxygen Consumption	Safe Period for Total Circulatory Occlusion
37C	100%	4 - 5 min.
29C	50%	8 - 10 min.
22C	25%	16 - 20 min.
16C	12%	32 - 40 min.
10C	6%	64 - 80 min.
6C	3%	128 - 160 min.

an experienced surgeon.

A lesser controversy has centered about the methods for cooling. Surface cooling has been advocated to be superior to core cooling due to less capillary shutdown, less tissue temperature variation and redistribution of blood flow and heat after arrest, less metabolic acidosis, and a shorter period of extracorporeal bypass.⁶

The basic principles of the hypothermic technique vary markedly from the usual principles of pediatric anesthesia at the Medical University of South Carolina which include: (1) no premedication except Atropine in infants under 6 months of age, the addition of small doses of barbiturates between 6 months and a year of age, and then the addition of narcotics over one year of age; (2) the avoidance of high concentrations of potent inhalation anesthetic agents (such as halothane); and (3) above all, attempts to keep the child warm. The principles of surface-induced profound hypothermia involve inhibition of reflex vasoconstriction with lytic cocktail premedication (a combination of promethazine, chlorpromazine, and meperidine), the use of potent inhalation anesthetics such as halothane, and above all, keeping the infant cold. The specific points of this technique are elaborated below.

The infants are premedicated with lytic cocktail 0.1cc/kg. If in extremely poor condition, the premedication is omitted or given in reduced dosage.

After arrival in the Operating Room, the infant is placed on a thermal blanket at 50 C. A precordial stethoscope and electrocardiograph leads are attached. An inhalation induction using a non-rebreathing technique with 50 per cent N₂O/O₂ and 0.5-1.0 per cent halothane is performed. When the infant loses consciousness, an intravenous catheter is placed and pancuronium (a neuro-muscular blocker) 0.1mg/kg is administered. After 3-5 minutes, the larynx is intubated using an uncuffed Portex nasotracheal tube. Arterial and central venous catheters are then inserted. Temperature is monitored by rectal and nasopharyngeal thermistors. Urine output is monitored via a foley catheter. D₅ .2NaCl is administered at 3cc/kg/hr with attempts to keep urine output greater than 0.5cc/kg/hr.

After the infant's condition has stabilized, bags of crushed ice are placed on the chest, abdomen, sides, and crown of head (See Figure 1). No ice is placed on the extremities due to fear of cold injury.⁷ When the temperature reaches 30 C, 2.5 per cent CO₂ is added to the anesthetic mixture to compensate for the respiratory alkalosis which results from a decrease in CO₂ production with low temperatures. If the systolic blood pressure falls below 40 torr, the concentration of halothane is reduced. Bradycardia (to a rate of 40) is common and has required no treatment. The cooling usually requires 1½-2 hours. At a temperature of 25-27 C, the ice is removed and surgery commences.

Heparin (3mg/kg) is administered, after which the aortic and atrial cannulas are placed. We are using an Olson pump oxygenator with a Bentley disposable infant bubble oxygenator. The prime consists of 1000cc of fresh heparinized blood and lactated ringers solution calculated to reduce the VPC to between 30 and 35. Sodium bicarbonate 5mEq and KCl 2mEq is added to the prime prior to bypass (based on Barratt-Boyes studies).

The oxygenator temperature is set at 4 degrees below the desired patient level

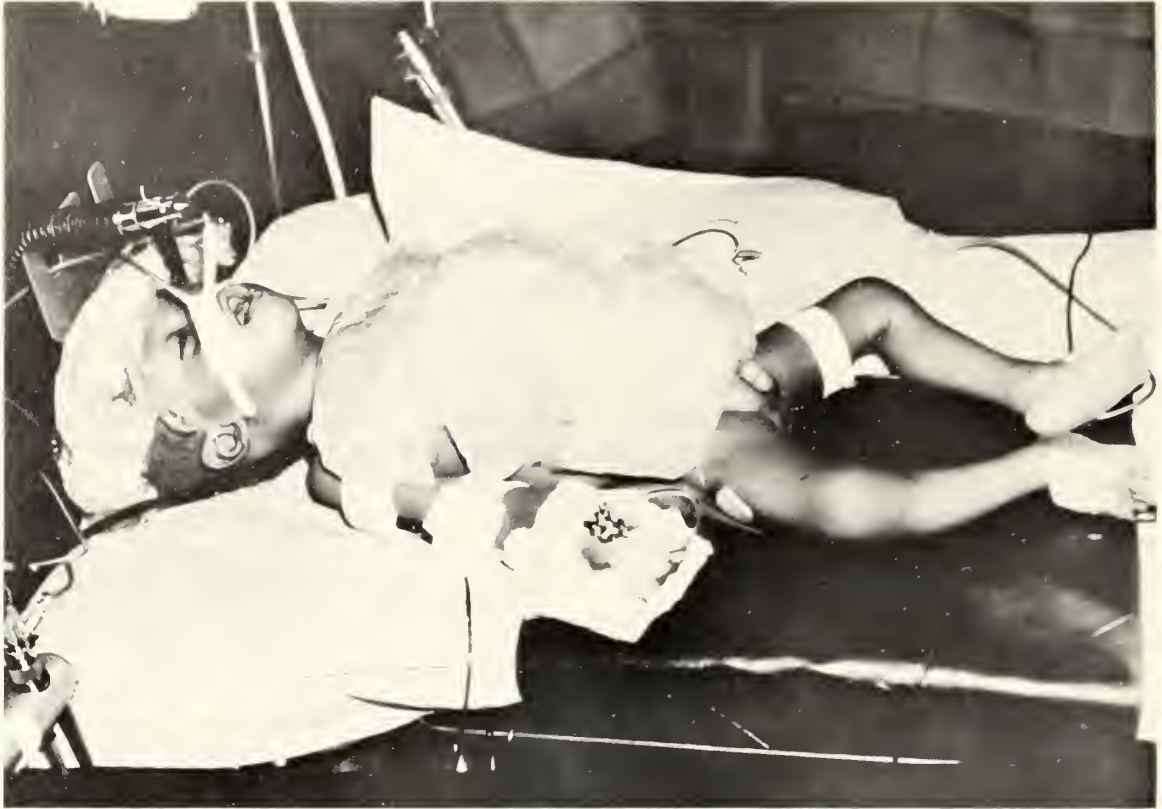


Fig. I Infant with ice bags applied

(usually 16 C). The infant is perfused at a flow rate of 50-100cc/kg until a temperature of 20 C nasopharyngeally is reached. The pump is then stopped, the aorta cross-clamped, and the infant allowed to exsanguinate through the atrial catheter into the oxygenator reservoir. The atrial catheter is then removed and the actual correction performed. During this time the lungs are statically inflated at 5cm water pressure (with 50% N₂O/O₂) to reduce the possibility of post-op pulmonary complications. When the surgery is completed, the atrial line is replaced, air aspirated from the heart and great vessels, and the aortic cross-clamp removed. NaHCO₃ 10mEq and KCl 2mEq are added to the prime and the temperature of the oxygenator set to 10 degrees above the current patient level.^{2,*} The thermal blanket is set at 37 C and warming begun. As warming progresses, warm ringers lactate is dripped slowly

onto the heart. Perfusion is performed at 50-100cc/kg/min. After restoration of normal cardiac rhythm, which is usually spontaneous but may occasionally require defibrillation, bypass is ceased at 34-35 C.

Core rewarming by ECC is used in order to avoid prolonged cardiac massage, to provide circulatory support if temporary arrhythmias should occur, and to allow more rapid correction of metabolic acidosis and return of organ function.^{2,*} When cardiorespiratory function has stabilized, protamine 6mg/kg is administered intravenously in divided doses. The continuing blood loss is replaced with pump blood via the aortic cannula. After cannula removal, fresh frozen plasma is administered for the first 100cc of blood loss. A mixture of 70 per cent fresh citrated blood (less than 24 hours) and 30 per cent fresh frozen plasma is administered for continuing blood loss in an attempt to keep the hematocrit in the

INTRACARDIAC DEFECTS IN INFANCY

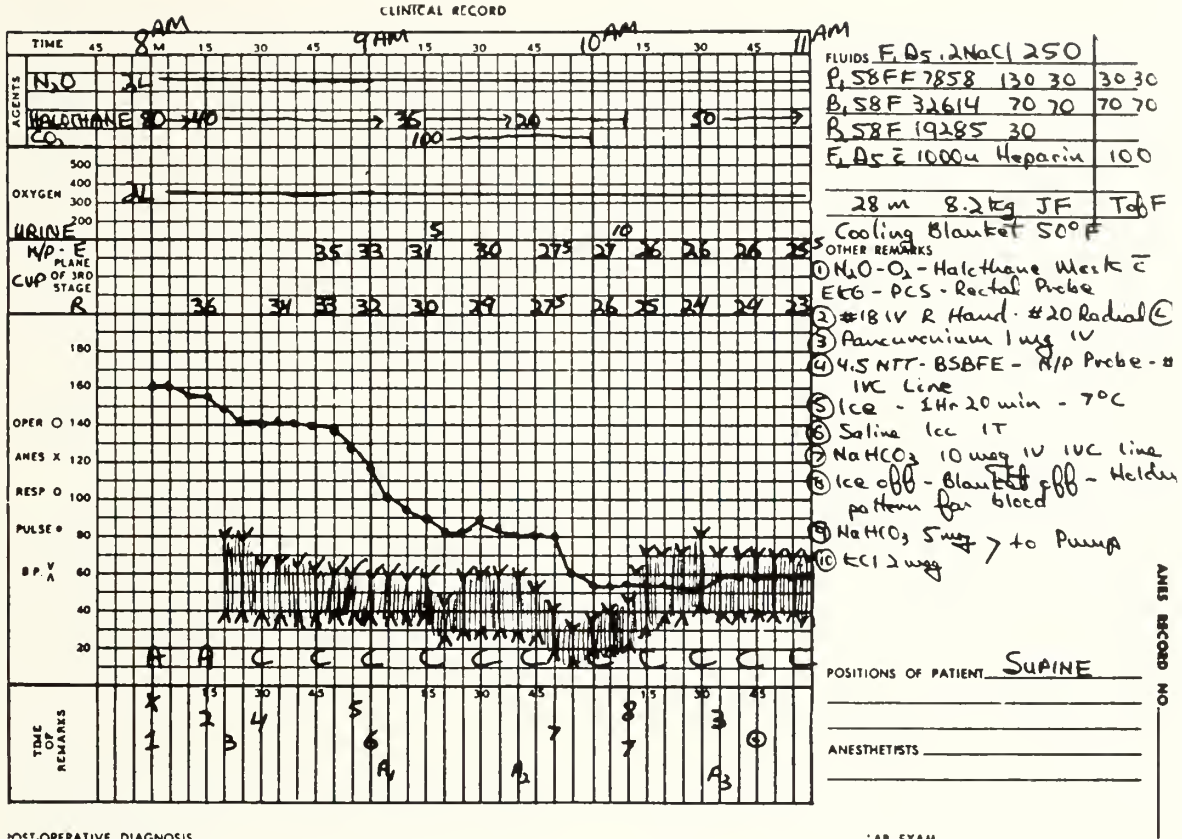


Fig. II Anesthesia record prior to arrest

30-35 range. CaCl₂ 10mg/kg is administered for every 100cc of citrated blood.^{6,7} At the end of surgery, the infant is taken to the intensive care unit, where all but one of the infants have been ventilated with either the Baby Bird or Emerson ventilators, with and without PEEP. Intermittant mandatory ventilation (IMV) is also used.

Figure 2 is a pre-arrest anesthetic record of a 28 month old, 8.2 kg infant with Tetralogy of Fallot. As cooling begins, the heart rate slows from the pre-induction rate of 170-180 to approximately 40-60 by the time surgery has commenced. As cooling progresses, the PR, QRS, and QT intervals become prolonged. We have had no difficulty with abnormal rhythms with the exception of occasional PVC's or junctional beats. Blood pressure remains remarkably stable. Decreases in blood pressure have responded immedi-

ately to a reduction in concentration of halothane. Even at extremely low temperatures cardiac function has been well maintained. The group at Toronto's Sick Childrens Hospital has reported that 6 infants (out of a total of 16) developed ventricular fibrillation prior to the completion of cooling to 25-27 degrees secondary to hypokalemia.⁴ This has not been our experience, but if serious arrhythmias should occur, the hypothermia allows time to commence bypass.

SUMMARY

Table II reveals data from our first 15 patients. These infants ranged in age from 4 days to 28 months and in weight from 3.7 to 8.2 kg. The duration of cardiac arrest varied from 38-77 minutes. The majority of the defects were transpositioning of the great vessels or Tetralogy of Fallot. There were 6 deaths in this series, with two of the deaths occurring in mori-

INTRACARDIAC DEFECTS IN INFANCY

TABLE II

PATIENT	AGE	WEIGHT ¹	DIAGNOSIS ²	PS ³	DURATION OF CIRCULATORY ARREST ⁴	N/P TEMP ⁵	DURATION OF ECC COOLING ⁴	DURATION OF ECC WARMING ⁴	DEATH ⁶
C.M.	3m	7.8	TGV	IV	52	20	11	36	
E.B.	9m	4.9	TGV/VSD	IV	67	20	12	24	
A.M.	8m	6.4	Tet	IV	57	18	12	40	
Z.M.	7m	3.7	VSD	IV	40	18	7	44	
D.B.	4d	4.9	VSD,Coarct,PDA	VE	38	20	10	70	20 min
C.B.	9m	6.0	TGV/VSD	IV	77	18	13	35	
J.M.	28m	8.2	Tet	IV	48	19	27	43	
J.C.	8m	8.0	Tet,ASD	VE	45	19	4	29	12 hours
K.S.	8m	5.4	DORV,VSD,PS	IV	62	19	6	39	3 days
W.W.	5m	4.6	VSD	IV	50	18	14	41	9 days
S.M.	3m	3.8	TGV	IVE	72	18	6	44	11 hours
T.M.	9m	6.8	DORV	IV	50	20	3	56	
S.F.	11m	6.0	VSD	IV	44	19	1	80	
J.O.	13d	3.7	TAPVR	IV	48	20	6	42	
A.B.	5m	7.7	ASD,PS	IV	40	19	7	52	32 hours

1 - Weight in Kg

2 - TGV=Transpositioning of the great vessels; Tet=Tetrology of Fallot; DORV=Double outlet right ventricle; TAPVR=Total anomalous pulmonary venous return; PS=Pulmonic stenosis

3 - Physical status

4 - Time in minutes

5 - Nasopharyngeal temp in °C

6 - No operative mortality-All post-op

TABLE III

AVERAGES FOR FIFTEEN INFANTS

Age: 7.5 months Duration of ECC
 Cooling: 9.3 minutes
 Weight: 5.9kg Warming: 45 minutes
 Arrest: 52.6 minutes Complications: 6.7%
 N/P Temp: 19°C Mortality: 40%

TABLE IV

PUBLISHED RESULTS

INVESTIGATOR	YEAR	NUMBER	MORTALITY
Dillard, Mohri	1971	31 Infants	45%
Barratt-Boyes	1971	41 Infants	20%
Kirkland	1972	21 Children	4.8%
Barratt-Boyes	1973	83 Infants	23%
Hisaka	1973	131 Children	13%

bund infants (physical status VE).

Table III reveals the averages for the infants in this series, while Table IV lists the results obtained by other investigators. Some of their cases involved older children and variations of this technique. There has been one complication in our first fifteen cases. One infant, who underwent repair of Tetralogy of Fallot, developed subglottic stenosis. The uncuffed Portex nasotracheal tube was in place for 4 days. There have been no renal, neurologic, or cold injury sequela in the survivors.

CONCLUSION

In conclusion, we do not advocate this technique as a panacea for the correction of congenital intracardiac defects in infancy; but, it has allowed a 30 per cent reduction in mortality (from 70% to 40%)

in infants who were not responding to medical management or palliative procedures. The technique may be the method of choice for correction of defects such as total anomalous venous return for which there is no medical therapy or palliative procedure. At the least, profound hypothermia with circulatory arrest adds another technique to the armamentarium of the cardiac surgeon, cardiologist, and anesthesiologist for the treatment of congenital heart disease in infancy.

ACKNOWLEDGEMENT

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CORONARY ARTERY SURGERY FOR IMPENDING MYOCARDIAL INFARCTION

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Coronary artery bypass has proven effective in the immediate restoration of blood flow to ischemic heart muscle with relief of angina pectoris,^{1,2,3} improvement in ventricular function,^{4,5} and prevention of subsequent myocardial damage.⁶ Naturally, interest has turned to applying the revascularization techniques for emergency intervention in patients with preinfarction angina.^{7,8,9,10} Fundamental to this approach is the premise that a recognizable stage in the evolution of ischemic heart disease exists when clinical signs suggest that infarction of the myocardium is pending.

This report is a critical analysis of a group of patients with preinfarction, unstable angina, categorized as high-risk in whom direct immediate myocardial revascularization was performed on an emergency basis.

MATERIALS AND METHODS

Patient Selection: Forty-four patients with preinfarction syndrome characterized by a combination of "high risk factors" and incapacitated by their illness were referred by the Cardiology Service at the Medical University Hospital for consideration of emergency coronary bypass surgery (Table I). These patients were considered high-risk on the basis of one or more of the following factors as determined by members of the Division of Cardiology at the Medical University

Hospital:

1. The presence of typical angina prolonged ischemic pain despite maximum therapeutic measures.
2. Crescendo angina in a patient previously free of symptoms.
3. Crescendo angina in a patient with prior stable angina.
4. Ischemic ST change during anginal episodes.

(All intractable to medical therapy for 48 hours.)

The patients were monitored in the Coronary Care Unit while undergoing the medical regimen consisting of bedrest, sedatives, narcotics, nasal oxygen, and coronary vasodilators. Anticoagulants were not routinely employed since surgery was frequently carried out within 72 hours of the patient's admission. Left heart catheterization including cineangiography by the Sones technique was routinely performed. A 70 per cent or greater obstruction of the coronary lumen was considered significant. The majority of patients had multiple vessel involvement and evidence of ventricular dysfunction. All patients were considered to be in Func-

TABLE I
SURGERY FOR PREINFARCTION
ANGINA
—PATIENT PROFILE—

Patients			
Age	No.	Sex	
30-39	7	Male	34
40-49	16	Female	10
50-59	10		
60 &	11	White	43
Total	44	Race	
(Avg. Age	50)	Negro	1

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tional Class IV of the New York Heart Association Classification. Factors considered significant in compounding the operative risks included diabetes in eight patients and hypertension in seven. None of the patients were in clinical congestive failure but five did manifest significant cardiac enlargement, and in 21 there was documented evidence of previous myocardial infarction.

Operative Technique: Suitable lengths of autogenous vein, generally the saphenous vein were obtained, with meticulous care and handling, through multiple incisions in the medial thigh and lower leg. The veins were irrigated with heparinized blood and gently distended to check for leaks. The proximal vein to aorta anastomosis was generally performed first utilizing a partial aortic occlusion clamp to create an elliptical aortotomy incision. The total cardiopulmonary bypass was employed along with moderate body hypothermia, and local cooling of the myocardium when ischemic cardiac arrest was necessary. The distal vein to artery anastomosis was performed by isolated occlusion of the coronary artery avoiding total myocardial ischemia whenever possible. All anastomoses were created with monofilament nylon in a continuous fashion.

Operative Procedures: One hundred four saphenous veins were inserted in the 44 patients with the majority of patients requiring more than a single graft. The internal mammary artery was utilized in two patients, one of whom had developed recurrence of angina attributed to occlusion of a vein graft previously placed to the left anterior descending coronary artery. Coronary endarterectomy was considered necessary in ten patients. Aortic or mitral valve replacement was required in two patients. Resection of a sizable ventricular aneurysm containing thrombus was performed in one patient.

Results (Table II): Thirty-eight patients (86%) are living 7 to 28 months following surgery. Twenty-six patients

TABLE II
SURGERY FOR PREINFARCTION
ANGINA

Living (7-27 Mo.)	38	(86%)
Hospital Deaths		
Intraoperative MI	1	
Four Days—CVA	1	
Eight days—Aneurysm		
Rupture	1	
18 Days—Myocardial		
Failure	1	
Total	4	(9%)
Late Deaths (15 Mo.)	1	
(25 Mo.)	1	(5%)

are free of angina and have discontinued all cardiac medication except digitalis. Eight patients expressed significant improvement of their angina with coincident reduction in the required medication and would be placed in the New York Heart Association Functional Classification Class II. Twenty-five patients are gainfully employed, and nine patients are either retired, living active lives, or else functioning in a capacity they consider normal without financial gain. Therefore, 89 per cent of the living patients are symptomatically improved following the operative procedure.

Myocardial infarction was documented by electrocardiography in six patients all within the perioperative period. Four of these patients manifested no symptoms, and five are included in the group of survivors who are gainfully employed.

Post-operative catheterization was performed in 11 patients for varying symptoms suggestive of myocardial ischemia. Patency was demonstrated in 17 (67%) of 25 grafts, but in ten of the 11 patients at least one graft was open.

A single intraoperative death occurred presumably secondary to a massive myocardial infarction in a female patient with severe diffuse occlusive disease requiring 3-vessel revascularization. Three other in-hospital deaths were encountered

at four, eight, and 18 days after surgery. Two late deaths occurred, one at 15 months and the other at 25 months, both in active asymptomatic patients who had resumed gainful employment. Autopsies were not obtained in either case.

DISCUSSION

Coronary artery bypass applied as emergency intervention in patients whose symptoms suggest impending myocardial infarction is gaining enthusiasm. The results of revascularizing the myocardium in these patients, although variable, have been significantly better than the results obtained in similar patient populations treated by medical regimen.^{11,12} However, a valid comparison awaits analysis of the treatment methods when they are applied to patients in whom there is uniformity of recognizable premonitory signs heralding impending myocardial damage.

The present study utilizes criteria described by Gazes¹³ in his ten-year follow-up of 140 non-operated patients with unstable angina. The high-risk subgroup identified on the basis of frequent angina in the hospital, prior stable angina, and ischemic ST change during pain, intractable to medical therapy for at least 48 hours was identified. The 12-month mor-

tality of this subgroup was 4.3 per cent. Thirty-five per cent developed a myocardial infarction within 3 months of the unstable angina with an associated mortality of 63 per cent.

The 44 patients included in the present study comprised a similar high risk subgroup established on the basis of identical criteria, with symptoms unremitting despite maximum therapeutic measures. Coronary bypass surgery performed as an emergency procedure yielded a 9 per cent hospital mortality and a 4.5 per cent late mortality reflecting a significant improvement in the prognosis of unstable angina with surgical management. Thirty-eight patients are living and, of the survivors, 89 per cent are either free of angina or significantly improved. In addition, these patients are either gainfully employed or pursuing an active life.

It is concluded that immediate direct coronary artery bypass for the relief of myocardial ischemia in a selected patient whose preinfarction unstable angina syndrome is characterized by a combination of high-risk factors affords considerable promise, especially when compared to a similar group in whom surgery was not performed.

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Ragan, C. The Clinical Picture of Rheumatoid Arthritis. in Arthritis. ed 8. edited by J. L. Hollander and D. J. McCarty. Jr. Philadelphia. Lea & Febiger. 1972. chap. 21. p. 335

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Important Note This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of fever, sore throat, oral lesions (symptoms of blood dyscrasia), dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications Children 14 years or less, senile patients, history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy, blood dyscrasias, renal, hepatic or cardiac dysfunction, hypertension; thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonamides, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions The following should be accomplished at regular intervals. Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions This is a potent drug, its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

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THE HYPERVISCOSITY SYNDROME

RICHARD SPROTT POLLITZER, M.D.*

The importance of the hyperviscosity syndrome has been well documented.^{1,2,3,4}

"If it is remembered that a man may die of an acute myocardial infarction or of a cerebrovascular accident without demonstrable thrombus in a coronary or cerebral artery at autopsy," state Burch and DePasquale, "the importance of 'rheology of blood which refuses to flow' becomes obvious."

"The practical physiological problems offered to the circulatory system by hyperviscous blood flow," says Williams, "have received surprisingly little attention from those interested in cardiac physiology in recent years."⁵

*Spartanburg, S. C.

It has been shown that the viscosity of blood in patients with infarction or thrombosis is higher than in normal controls.⁶

For years, determination of viscosity has been performed by European investigators, using the viscometer.⁷

The hyperviscosity syndrome may be due to several disorders, as shown in Figure 1, and as outlined below.

- I. Paraproteinemias: possibly the electrical charges from the large protein molecules attract oppositely charged erythrocytes, leading to rouleau formation and an increase in viscosity:
 - A. Macroglobulinemia.
 - B. Cryoglobulinemia.

HYPER-VISCOSITY SYNDROMES

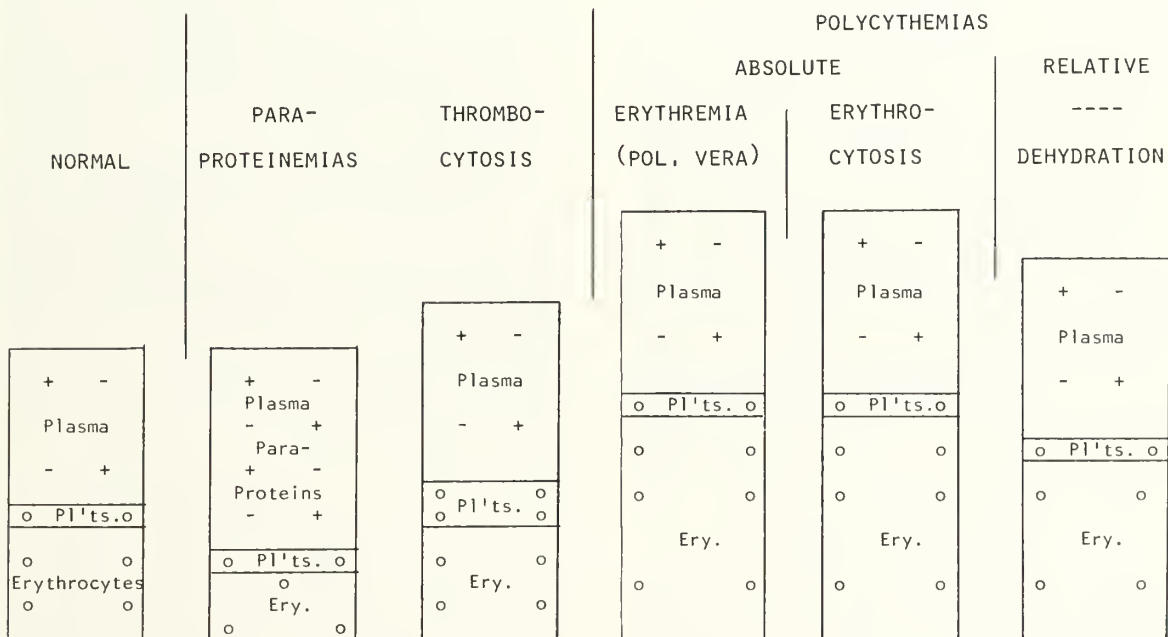


Figure 1

- C. Multiple myeloma.
- II. Thrombocytosis: increase in platelets with combination of electrical and mechanical effects, plus coagulation factors:
 - A. Thrombocytosis.
 - B. Thrombocythemia.
- III. Polycythemias: mechanical effect of increased numbers of red cells.
 - A. Absolute (increased total red cell mass).
 - 1. Erythremia ("polycythemia vera").
 - 2. Erythrocytosis (polycythemia secondary to pulmonary disease, right-to-left shunt, etc.)
 - B. Relative (increase in red cells per milliliter of blood, due to *increase* in plasma volume).

In clinical practice one often sees *combinations* of the above entities. In our experience over about a decade, measurement of the viscosity of the blood has proven a useful procedure.

METHOD

We use an Ostwald Viscometer (Cannon-Fenske modification), which is a very narrow glass tube, surmounted by a bulb. All determinations are done in a water bath at 37°C. To calibrate the viscometer, the bulb is filled with distilled water; the time required for the bulb to empty through the narrow tube is designated 1 "relative viscosity unit." The viscometer is then thoroughly dried. Blood from the patient is obtained in ordinary anticoagulant tubes, and tested in a similar manner. In our laboratory, the time required for normal blood is approximately 5 to 6 times that of water, hence "normal" for blood is 5 to 6 relative viscosity units. This compares fairly closely with normals given by Wintrobe (3.5 to 5.4 units).⁷

CASE HISTORIES

Several physicians in upper South Carolina have kindly referred to us a number of cases which were found to have the hyperviscosity syndrome.

I. A man, 69 years old, was referred to us in 1965 by Dr. W. A. Wallace of Spartanburg. The

patient, who was the father of a physician, complained of chest discomfort, dyspnea, and weakness. His skin was pale; retinal examination showed "exudates and dilated veins." Hemoglobin was only 10.3 grams, but our technician recorded "blood very thick." Erythrocytes showed rouleaux. Gammaglobulin was elevated. Dr. Michael Patton, Pathologist at the Spartanburg General Hospital, suggested the diagnosis of macroglobulinemia (an example of paraproteinemias). The patient was transferred to the Cleveland Clinic, where he was seen by Dr. James S. Hewlett. Ultracentrifuge studies of serum showed 39.2 per cent 19S, 8 per cent 27S, and 4.9 per cent 35S macroglobulins. Relative blood viscosity was 39 units (all subsequent viscosity determinations reported in this paper were done in our laboratory).

After performing plasmapheresis, Dr. Hewlett started the patient on steroids and Chlorambucil. Viscosity declined to normal in a few months. Over a decade of observation, the patient has done well. This patient illustrates the development of hyperviscosity due to alterations in the plasma proteins from a paraproteinemia; also illustrated is the fact that the hemoglobin and hematocrit are not a reliable guide to hyperviscosity.

II. A 49-year-old man was referred to us by Dr. Guy Blakely of Woodruff, S. C., because of the history of melena and anemia, which had been followed by a rise in hemoglobin and leukocyte count. The platelet count was elevated to 1,000,000 per cubic millimeter. Leukocyte count was 39,000 cells, of which 90 per cent were Neutrophils. Bone marrow showed generalized hyperplasia with "rubricytic or leukemoid reaction," and thrombocytosis. Relative blood viscosity was 17.5 units.

On Busulfan, relative viscosity dropped to 7.8 units. Therapy was given intermittently. Some months later, the patient had an episode of hemoptysis; platelet count was 2,390,000. Busulfan was resumed, with rapid improvement. On follow-up exam, approximately four years after initiation of therapy, the patient's condition was satisfactory.

This is probably an illustration of the hyperviscosity syndrome due to an increase in platelets (thrombocytosis).

III. A woman, age 64, was referred to us by Dr. William Hendrix, of Spartanburg, because of paralysis of the left arm. Neurological evaluation was suggestive of cerebral thrombosis. The face and mucous membranes were very red. Retinal veins appeared dilated. Just prior to our seeing the patient, Dr. Hendrix had obtained a hemoglobin "greater than 20 grams." Blood volume was 5696 mls. (predicted 4000 mls.). Bone marrow examination showed production of large numbers of platelets; there was also evidence of poly-

cythemia. Relative viscosity was 12 units. Treatment consisted of repeated venesection; later, radioactive phosphorus was given. The relative viscosity dropped to 6.6 units. A few years later, she complained of weakness and vertigo; her relative viscosity was found to have risen to 10 units, and her hematocrit to 63 per cent. Venesection again resulted in improvement; she was maintained on Busufan intermittently and later given radioactive phosphorus again. The patient has continued to do well, on this regimen, for a decade. This case illustrates a combination of thrombocythemia and erythremia ("polycythemia vera"), and shows the value of viscometry as a guide to therapy.

IV. A 70-year-old insurance man complained of numbness of his fingers. His past history included gangrene of the left leg some years previously. Our examination showed redness of the skin and mucous membranes; retinal veins were dilated, and the spleen was enlarged. The hematocrit was 7.1 per cent, hgb. 18 grams, blood volume was 7679 mls. (predicted 5500 ml.). Bone marrow was compatible with polycythemia vera. Relative viscosity was 10.5 units. Venesection and radioactive phosphorus produced considerable improvement. This patient illustrates erythremia, and again demonstrates the value of viscometry.

V. A 53-year-old textile worker was referred to us by Dr. George Hughston because of pain in the anterior chest, dyspnea, and cough. He had had status asthmaticus some months earlier, with myocardial failure and hyperglycemia.

Examination showed a dyspneic, obese man, with plethora. The optic fundi showed dilated retinal veins. The heart appeared enlarged; lungs exhibited expiratory wheezes.

Hemoglobin was 19.1 grams; hematocrit 55.9 per cent; blood volume 7060 ml (predicted 5420 ml). Total red cell volume was 4120 ml (predicted 2515 ml).

Relative blood viscosity was elevated to 8.2 units. The vital capacity was only 1.3 liters (predicted 3.74 liters). One-second capacity was only 0.51 liters (predicted 2.9 liters). These findings were interpreted as indicating severe ventilatory impairment of restrictive and obstructive type.

The patient was digitalized and was given Aminophyllin preparations. He was advised to donate blood at a blood bank.

This case illustrates the hyperviscosity syndrome due to erythrocytosis (polycythemia secondary to pulmonary disease).

VI. A 30-year-old mongoloid man was admitted complaining of severe dyspnea, orthopnea, and cough. The lungs exhibited inspiratory rales and expiratory wheezes. The skin appeared dehydrated.

Hemoglobin was 17 grams; hematocrit was 59 per cent. Plasma volume was only 40 per cent

of total blood volume. Relative viscosity was 8.2 units. Therapy included hydration with intravenous fluids.

This case may illustrate the hyperviscosity syndrome due to simple dehydration (relative increase in red cells per ml. of blood, due to decrease in plasma volume, secondary to inadequate fluid intake, or excessive loss of fluid).

DISCUSSION

Symptoms of the hyperviscosity syndrome include chest pain, dyspnea, headache, vertigo, paresthesias. These patients are often mislabeled as neurotic until adequate studies are made.

Physical signs may also be misleading. Although the skin and mucous membranes may be plethoric in the polycythemias, pallor may be the outstanding finding in the paraproteinemias. The spleen may be enlarged in the polycythemias.

Laboratory findings may also be confusing. The sedimentation rate is likely to be normal in any of the hyperviscosity syndromes. The hematocrit and hemoglobin are *not* useful parameters; they may be elevated in the polycythemias, but may be low in the paraproteinemias. Viscometry provides more direct information regarding diagnosis and therapy.

The biophysical basis of viscometry is simple. Rate of flow (F) is inversely proportional to the viscosity (V); this is expressed in the formula: $F = \frac{1}{V}$.

This formula was further elaborated a century ago by Poiseuille⁸ for blood vessels or other tubes, using the abbreviation P_1 for pressures at the proximal end of the tube, P_2 for pressures at the distal end, and $P_1 - P_2$ for differences in pressure. He showed that the correction factor of $\frac{\pi}{8}$ was necessary. The complete Poiseuille formula is $F = \frac{(P_1 - P_2) R^4}{8V}$.

SUMMARY

The hyperviscosity syndrome is fairly common. Etiologic entities include polycythemias, thrombocytoses, and paraproteinemias. Pathogenesis involves increases in cells, platelets or large protein molecules. Symptoms include chest pain, dyspnea, and paresthesias. Physical signs

HYPERVISCOSITY SYNDROME

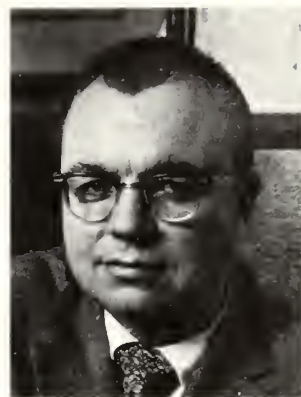
may be misleading, since there may be plethora or pallor; probably the most significant physical findings is dilatation of the retinal veins.

The viscometer is a simple, inexpensive device, which can be used in the physician's office for diagnostic screening of patients, and monitoring of therapy.

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President's Pages



Professional Liability Insurance—An Endangered Species?

All South Carolina doctors are familiar to a variable degree that professional liability is a worrisome problem. But most doctors who have not looked at the national scene recently do not realize how severe a problem professional liability insurance really is. Consider the following facts:

A) Since 1930, 416 malpractice suits have been filed in Indiana. This might not sound so alarming in itself, but for the fact that 265 of them have been filed in the last *five* years, accounting for 81% of the total dollar amount sought by claims. Anesthesiologists in Indiana saw their rates go from \$3,000 to \$15,600 this past year.

B) In Michigan, no doctor starting in practice after January 1, 1975, will be insured by the two companies remaining in the state.

C) In California, anesthesiologists, orthopedic surgeons, and obstetricians and gynecologists are paying currently \$6,000 a year for the average premium. But when renewal time comes, one insurance company says charges will average \$25,000 a year; and other companies are contemplating major rate increases.

D) In New York, rates were already as high as \$15,000 a year for some specialties in terms agreed upon only last July. But the Argonaut Insurance Company stated that they would not insure after July 1, 1975, unless the state insurance commission agreed to triple their rates; and some specialties are paying up to \$42,000 yearly for renewals.

E) In Maryland, doctors have only until April 30th, to find another carrier when St. Paul Insurance Company pulls out.

F) Here in South Carolina there is only one major carrier of professional liability insurance, St. Paul, who recently got an 82% increase in rates. Other carriers are rapidly pulling out of South Carolina.

Professional liability has become a walking disaster largely because the American public does not recognize the problem in which its own interests are at stake. Most people believe that professional liability is a problem concerning only physicians, hospitals, and insurance companies. And it is true that the most immediate effect is felt by physicians and hospitals in the form of premium costs. But the ultimate effect, both in terms of monetary costs and the quality of care, falls directly and most heavily upon

the public. When premium rates double, triple and even quadruple, physicians and hospitals protest. But we pay—and we pass the additional costs along in the form of higher fees and higher rates because we have no other choice. The final person who pays—and the real loser—is the public, the individual patient. When insurance companies pull out or threaten to pull out of the state, it is the American public—the individual patient—who is threatened with loss of care. For what physician in his right mind would dare see a patient without liability protection? And even when a physician can get protection at exorbitant costs, there is another indirect cost to the patient. A physician shortage is accentuated at both extremes of age. The young physician coming just out of his residency program and usually several thousand dollars in debt, is faced with a \$25,000 professional liability premium. Do you think he practices in this state? No, he heads for one of the few remaining states with fairly reasonably priced professional liability premiums or goes to work for the Veteran's Administration or some other government agency or an insurance company. At the other end of the spectrum is a physician approaching retirement who desires to taper off in his practice. A surgeon performing 600 operations a year possibly may be able to pay \$25,000 a year for professional liability premiums, *if* he can spread it out over a large practice. But a surgeon working 3 days a week performing 50 or 60 operations a year may well decide to accelerate his retirement rather than pay such an exorbitant premium which he might well find impossible to get from his patients in extra fees, even if he desired to do so.

An extra expense is also found in hospitals. The Long Beach Memorial Hospital in California 10 years ago paid \$14,000 a year in professional liability premiums. In 1966, it was \$47,000 a year; in 1971 the cost had risen to \$160,000 a year; in 1974 the cost was \$340,000 a year; and in January 1975, Long Beach Memorial Hospital was told that its premiums would be \$820,000. What does all this mean to the patient in terms of cost? In 1965 the cost per patient per day to cover the professional liability premium was 10¢. In 1975, each patient in Long Beach Memorial Hospital will pay \$3.65 every day to cover the cost of professional liability premiums.

And what does the patient get in return for this investment of his money? Only 16¢ out of every dollar spent for professional liability insurance ends up as direct benefits to patients who suffer medical injuries! All the rest—84¢—goes for plaintiff and defense lawyers, for the costs of investigation, for medical witness fees, for insurance underwriting costs, and salesmen's commissions. The cost of such a system is outrageously extravagant and clearly wasteful. What we need is a system that protects the public without gouging, a system that recognizes legitimate medical injury, a system that takes care of those who are injured without unusual delay, and at a rate commensurate with the seriousness of the injury.

One other reason that the threat of professional liability suits add to the cost for the patient is that physicians, by fear of malpractice, reduce their medical practice to a cookbook approach. Forced compliance with one method of treatment caused the stagnation of Babylonian and Egyptian medicine. There is no more deadly threat to medicine and medical progress than this. Not only are unnecessary X-rays, laboratory tests, and other procedures done; but almost all progress, certainly all revolutionary progress, is going to be achieved by going against the prevailing concepts of the time. History has so many examples of this, Copernicus, Galileo, Newton, Einstein—and in the medical field Pare, Lister, Semmelweis, Pasteur, Walter Reed, that it hardly needs to be mentioned. Progress is achieved by going outside customary and usual procedures. It derives from the freedom to experiment and to innovate. It derives not merely from the freedom to succeed but equally from the freedom to fail.

This then is the problem! What are some of the possible answers?

A) If all professional liability insurance goes or professional liability insurance becomes prohibitively expensive in South Carolina, all doctors might be forced to add a surcharge on all fees to set up a financial reserve to pay off professional liability costs. This is not a very satisfactory solution, because it would be hideously expensive for the public and cumbersome to manage for physicians.

B) The State of South Carolina might set up a malpractice pool, something akin to the old assigned risk driver's pool, to force all insurance companies who do business in the state to take a part of the business. However, we physicians believe that such a program would be grossly unjust to insurance companies. Any law that would force a company to operate at a loss is repugnant to any fair minded physician. Besides, in the backlash, insurance companies might refuse to do business with South Carolina and totally wreck the insurance industry in this state.

C) The final possibility, and one which I believe merits the most consideration, would be legislation in South Carolina which would guarantee the patient a fair deal yet cut out most of the factors which make South Carolina an unattractive state for professional liability insurance carriers.

- 1) That awards for pain and suffering and punitive damages should be limited or totally removed as an item for monetary damages as in the case of Workman's Compensation and Automobile No Fault statutes.

- 2) The medical costs already paid for by Medicare, Medicaid, and other third parties be excluded as part of the court's award. Under existing law, a successful malpractice claimant can recover for medical and hospital costs that already have been paid for by these third parties. Certainly such payments would be eliminated under a federally administered national health insurance system.

- 3) The elimination of windfall recoveries. Recovery should be allowed for out-of-pocket medical and other applicable expenses from the date of occurrence to the date of settlement. Funds should be set aside to handle such future expenses on a continuing basis through the establishment of "reversionary trusts." This arrangement would prevent situations where persons other than the injured party profit from large lump sum settlements.

- 4) There should be a ceiling on damages established on a reasonable basis comparable to Workman's Compensation.

- 5) Some consideration needs to be given to shortening our statute of limitations. We are the only state in the Union that has a 6 year statute of limitations. Only 14 states have a statute of limitations more than 2 years. When you add on to this the possibility of waiting until a child reaches his majority, it is easy to see why malpractice insurance rates are very difficult for insurance companies to calculate.

- 6) The contingency fee system is open to many abuses. Only in the United States do you have such a unique all-or-nothing gamble. However, it is recognized that our present system of contingency fees gives a poor person his right to have a day in court that would be impossible otherwise. However, it would be more fair to seek legislation such as exists in New Jersey where there is a sliding scale for contingency fees. In other words, as the size of the award increases, the contingency fee decreases proportionately.

7) The *Ad Damnum* clause in lawsuits should be eliminated, therefore preventing the amount of damages sought from being specified. Almost always, the large amount specified in complaints is not recovered. Nevertheless, publication of the amount of damages being sought has the same practical effect as publishing the amounts of large recoveries. In both instances, such actions serve to encourage litigation.

8) The establishment of a state mediation system for small claims similar to legislation passed in New York State Legislature should be considered. It still does not deny a plaintiff his chance in court, but gives speedy settlement in relatively minor cases and cuts down on the time and expense involved.

In the immediate future we will be talking with the South Carolina Legislature about adopting this final method. It is not too late in South Carolina as it is in most states. Although it is not 3 minutes until midnight, I think it is well past 10 o'clock; and we physicians had better act before the coach-and-four turns back into pumpkins and mice. We are the victims of an unfair system; and while it is true that we physicians will suffer, it is the public that will suffer the most if we do not act.

Donald G. Kilgore, Jr., M.D., President
South Carolina Medical Association

Editorials

1985

Just as miles are insignificant in measuring interstellar distances, dollars are insignificant in measuring profit of the Arab oil block nations in the world today. Scientists developed the light year to define distances in space. The London *Economist* recently published an article devising the "profit-year" to represent the number of dollars profit to the Oil-block in one year. This measure was applied to several areas, with chilling results.

One and a half profit-years could purchase the United States' entire overseas investments. Two profit-years could acquire all issues on the London Stock Exchange and two and a half profit-years would wipe out the New York Stock Exchange. Most significant of all, ten and one half profit-years equal all the capital in the world. In other words, at the present rate, in 1985 the Arab oil block nations will own all the capital in the world!

This is not a medical problem but is a problem of such overriding and worldwide significance that we need to be aware of it and start learning to live within our means.

George Orwell's "1984" is bleak but this 1985 would be much worse.

EEK

Where Do Our Taxes Go? And Why?

\$378,000 to study flight characteristics of the Frisbee

\$87,000 to study the smell of Australian Aboriginal perspiration

\$85,000 to assess the impact of rural road construction in Poland

\$35,000 to study the habits of wild boars in Pakistan

\$71,000 to complete a history of comic books

Do any of these expenditures offend or irritate you? The National Taxpayers Union recently released a report on how tax dollars are spent showing the above projects. It looks like we need some system of quality control on such expenditures of OUR money! We worked hard for this money and don't want it thrown away on silly and unproductive projects. Right? If you agree, read on, I may have caught you in a little trap.

\$8 for 50 terramycin capsules to treat a cold

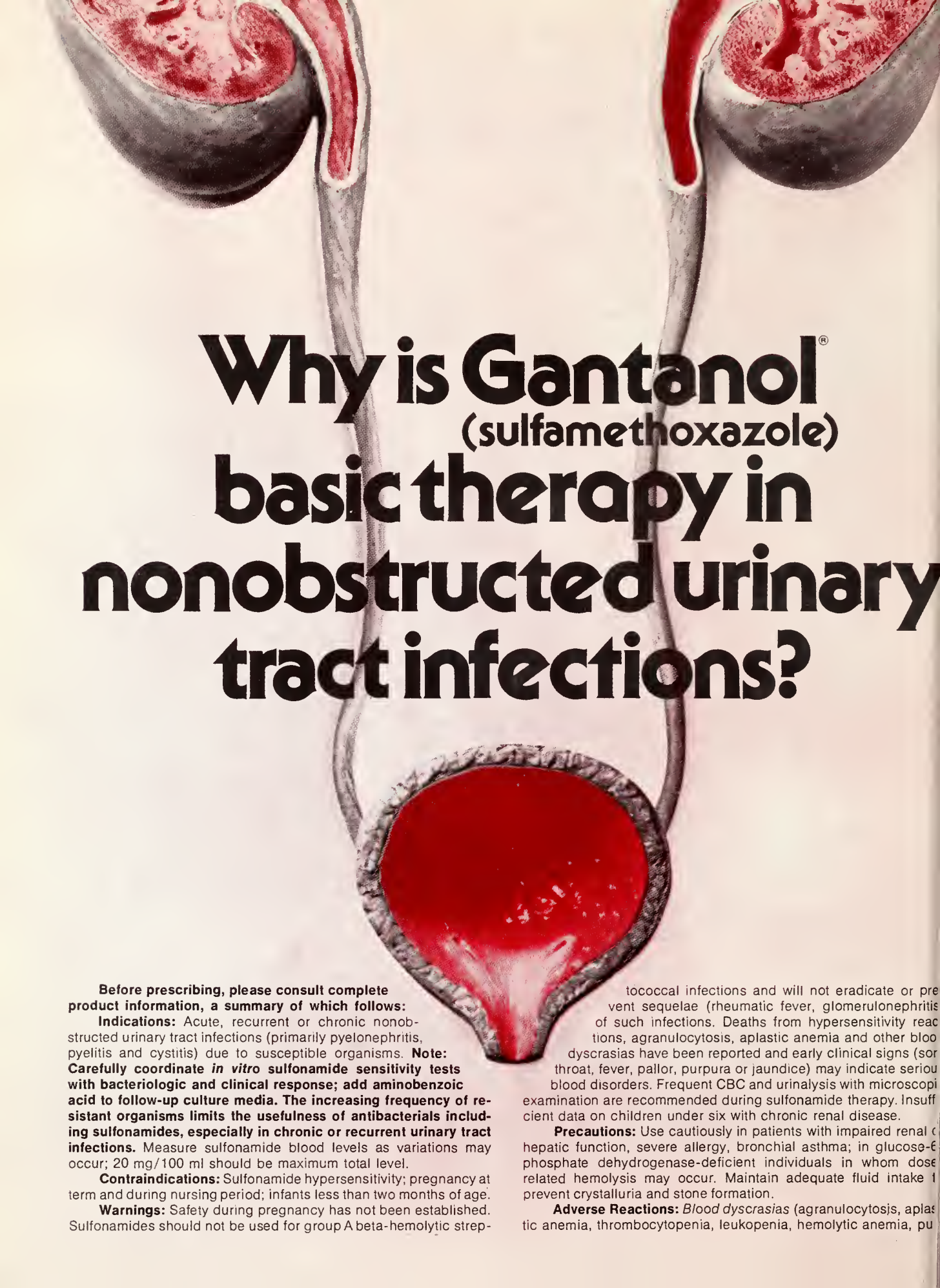
\$7500 to one surgeon for 15 "hiatal hernia repairs" in a year's time

\$120 for daily "B12 shots" for 2 months for a 69-year-old woman with low blood.

\$683 for a 10-day hospitalization for a man with "pneumonia." All physical, lab, x-ray findings normal and patient afebrile throughout.

Any of these needless expenditures offend you? True, the individual amounts are not great, but extend the list and multiply it by thousands, and we see millions of wasted tax dollars. Perhaps we need a system of quality control of Medicare, Medicaid, and maternal and child health program expenditures, because many billions of tax dollars are involved each year. Perhaps PSRO is the best system yet available. Do you have a better one to suggest?

EEK



Why is Gantanol[®] (sulfamethoxazole) basic therapy in nonobstructed urinary tract infections?

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. **Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic strep-

tococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, pu-

Because it is considered a good choice...

- for efficacy in nonobstructed cystitis, pyelonephritis and pyelitis
- for control of susceptible *E. coli*, *Klebsiella-Aerobacter*, *Staph. aureus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*
- for prompt antibacterial blood and urine levels in from 2 to 3 hours after initial 2-gram adult dose
- for economical around-the-clock coverage
- for maximum patient cooperation with easy-to-remember B.I.D. dosage

Basic Therapy **Gantanol[®]** (sulfamethoxazole) Tablets/Suspension (0.5 Gm) (0.5 Gm/teasp.)

pura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasps.) Initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasps.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110



50 YEARS AGO

February 1925

Considerable progress was reported in organizing women's auxiliaries in the county societies of the state. On the subject of roentgenology Dr. T. A. Pitts of Columbia discussed the increasing recognition of thymic enlargement and the successful use of the x-ray in its treatment.

9th ANNUAL OPHTHALMOLOGY RESIDENTS CONFERENCE MEDICAL UNIVERSITY OF SOUTH CAROLINA APRIL 10-12, 1975

Guest speakers:

Paul Henkind, Bronx, N.Y.

Dan B. Jones, Houston, Tex.

Herbert E. Kaufman, Gainesville, Fla.

Residents and attending staff will also present papers.

Registration fee: \$30.00

(Does not include social functions)

For additional information, write:

Staff Assistant

Department of Ophthalmology

Medical University of S. C.

80 Barre St.

Charleston, S. C. 29401

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdose or individual hypersensitivity, reactions similar to those after meperidine or morphine overdose may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdose; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdose may cause severe, even fatal, respiratory depression. Signs of overdose include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE

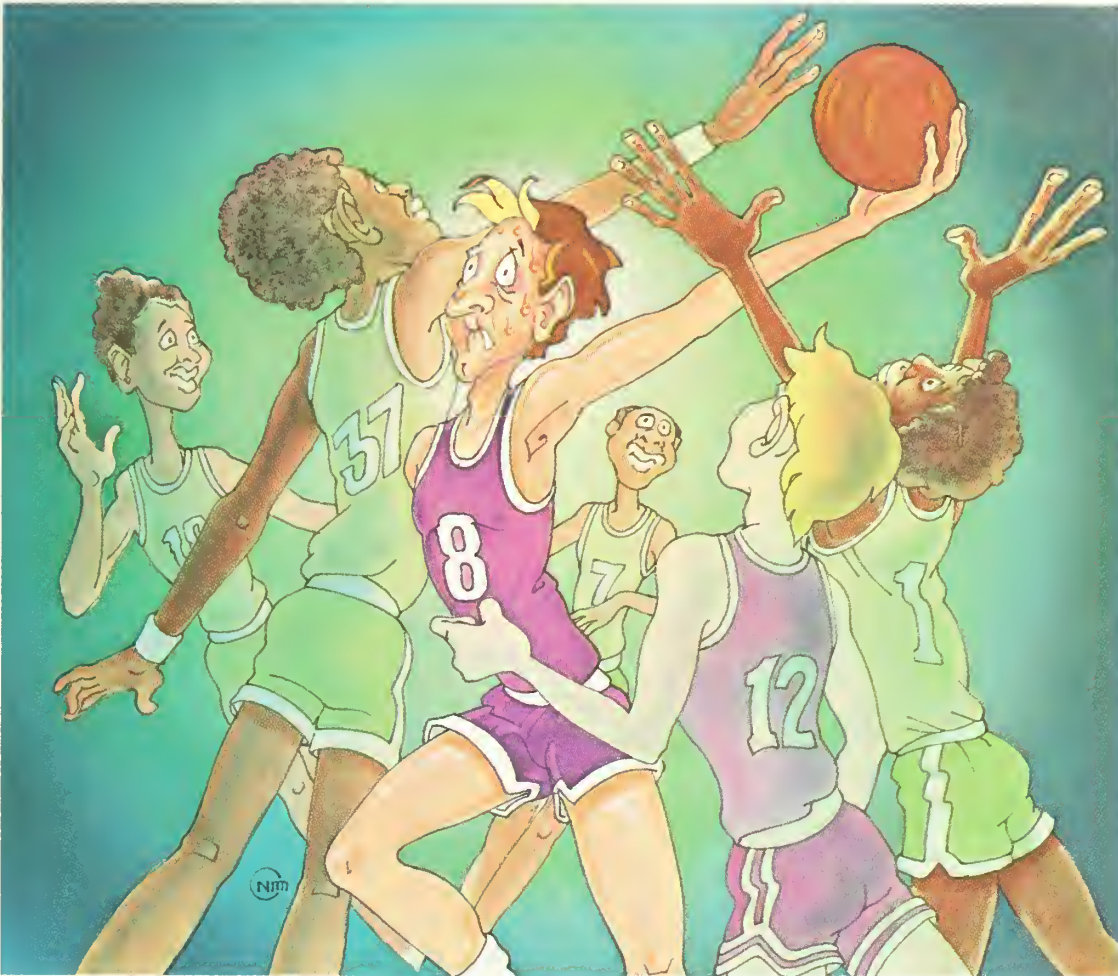
Searle & Co.

San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

454 R

When diarrhea has his number...



Lomotil puts him back in the game.

Physicians and patients both want prompt control of the symptoms of diarrhea. A rapid, uncontrolled loss of fluids and electrolytes can cause a medical crisis, particularly in children, and in patients who are seriously ill, or in people who are badly undernourished.

Lomotil usually stops diarrhea promptly. This rapid action halts the emergency aspect of diarrhea

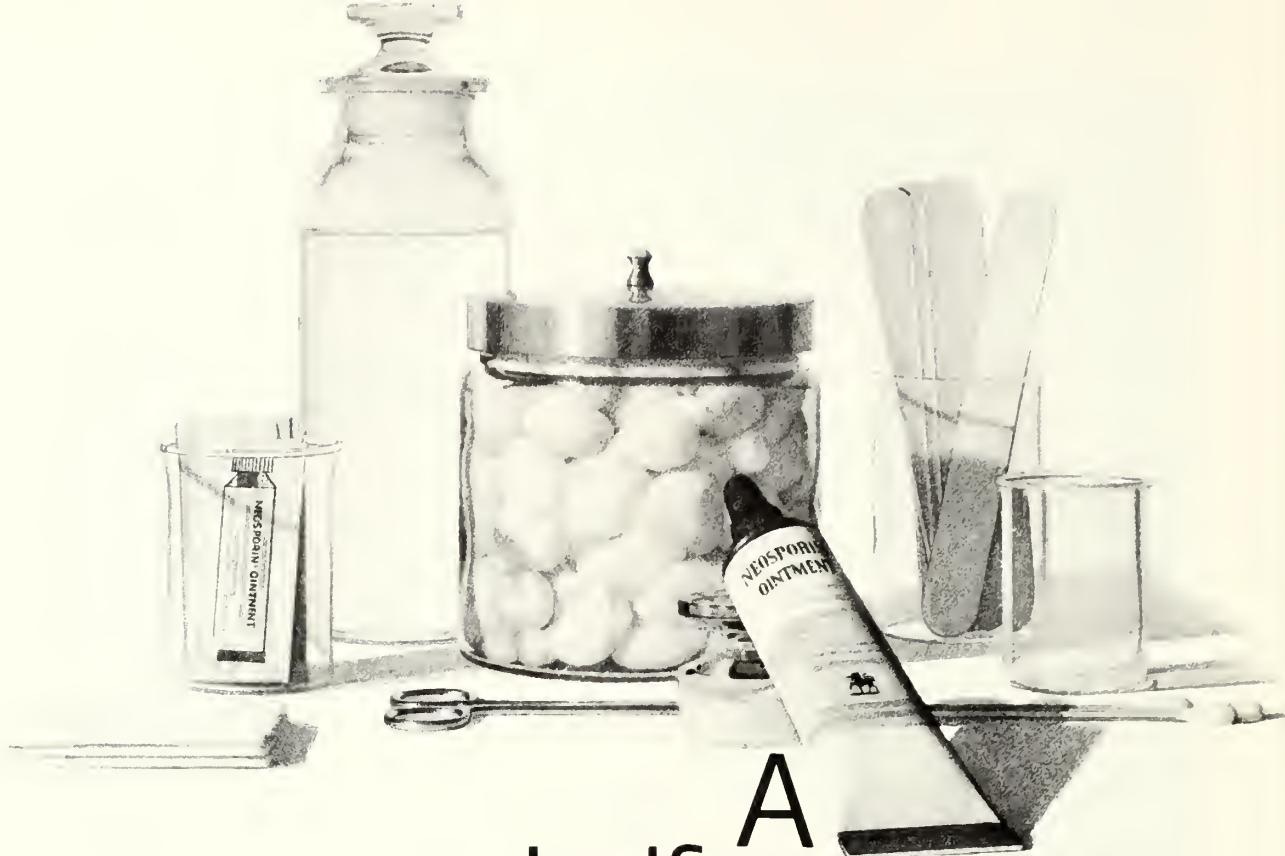
and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate antibiotic therapy should be given along with Lomotil.

Lomotil has few side effects, and those that do occur are generally mild.

Lomotil[®]
TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride 2.5 mg
(Warning: May be habit forming)
atropine sulfate 0.025 mg

Usually stops diarrhea promptly.



A half-ounce of prevention

Use it to prevent a topical infection. Or to treat one that's already started.

In either case, it's good medicine. Whether for lacerations, burns, open wounds, IV catheter or surgical aftercare.

Neosporin® Ointment provides broad antibacterial coverage against common susceptible pathogens. And since it contains three antibiotics that are rarely used systemically, the risk of sensitization is reduced.

Neosporin Ointment. A half-ounce of prevention. Also available in a full ounce of prevention and in convenient foil packets.

Neosporin Ointment carried on Apollo and Skylab missions.

Neosporin® Ointment (polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs.
In tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa

• primary pyoderimas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis)

• traumatic lesions, inflamed or suppurating as a result of bacterial infection.
Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. P



Wellcome

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities.

Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F CO.
Carolina, P.R. 00630
Subsidiary of
SmithKline Corporation

KEEP THE HYPERTENSIVE PATIENT ON THERAPY KEEP THERAPY SIMPLE WITH **DYAZIDE**[®]

Trademark

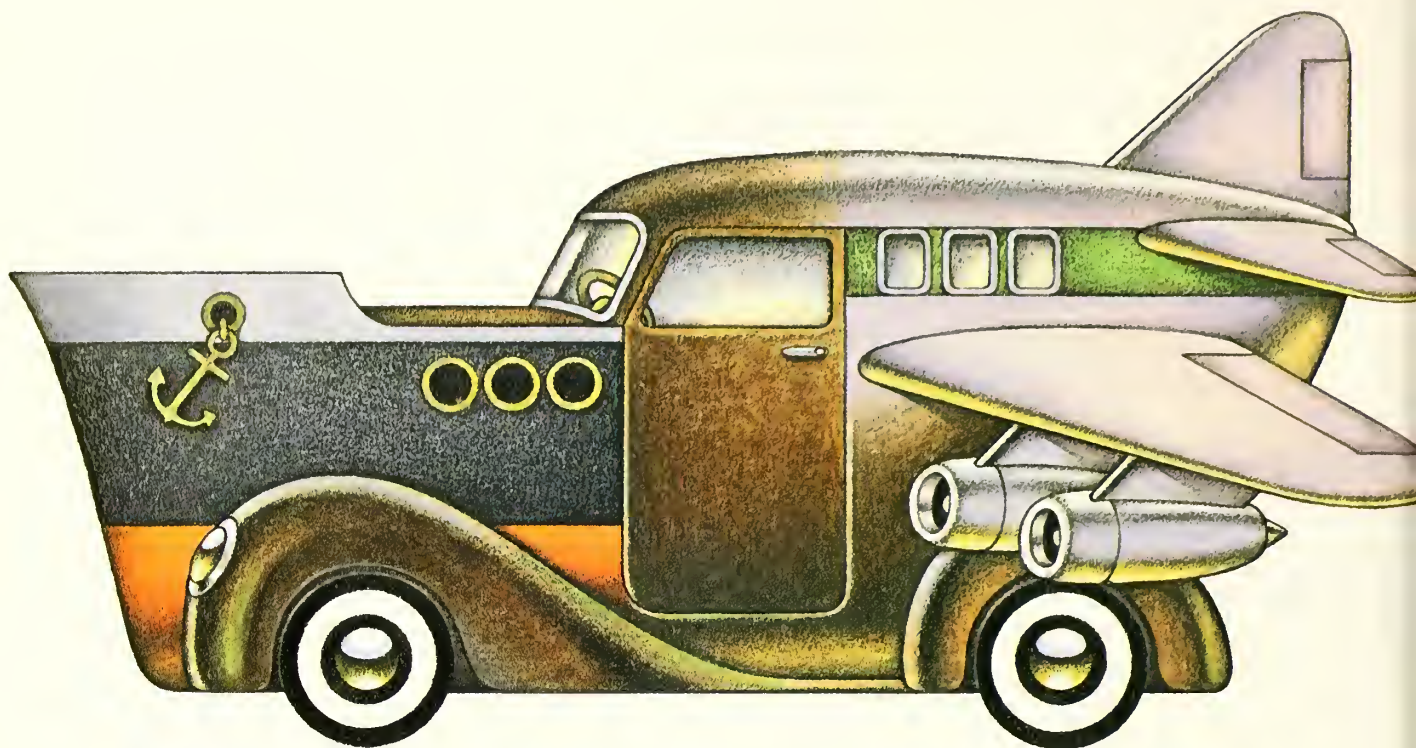
Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Neither inconvenient potassium supplements
nor special K⁺ rich diets needed as a rule.
Just 'Dyazide' once or twice daily for maintenance.



Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP



On land, sea, and in the air...

Up to 24 hours of effective control with a single dose...in nausea, vomiting and dizziness associated with motion sickness.

Dosage: 25 to 50 mg. 1 hour before travel.

Available on prescription only.

BRIEF SUMMARY OF PRESCRIBING INFORMATION
CONTRAINDICATIONS. Administration of Antivert during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did

not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

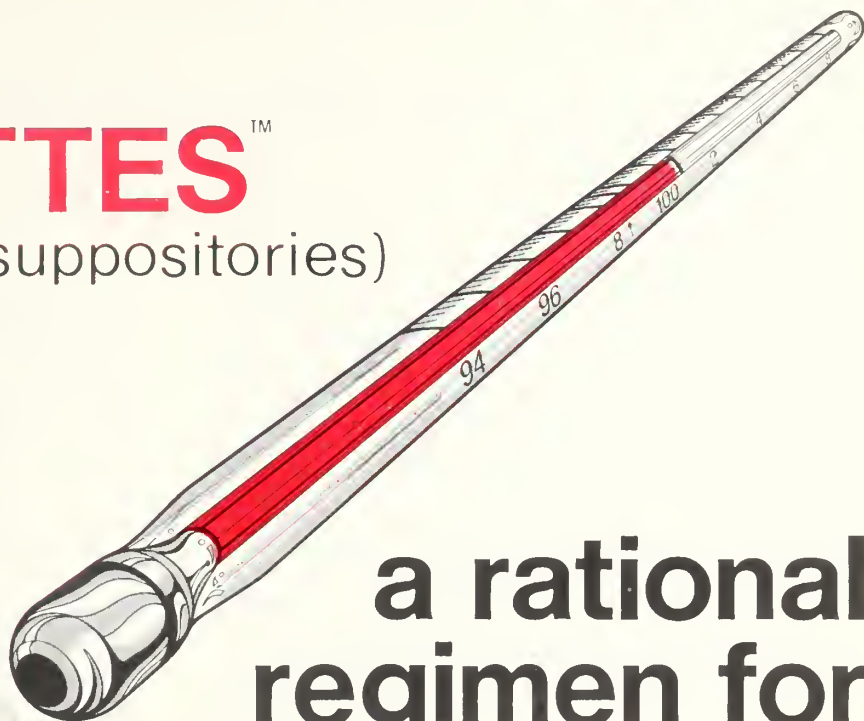
ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

ROERIG 
 A division of Pfizer Pharmaceuticals
 New York, New York 10017

Antivert®/25 Chewable Tablets
(meclizine HCl) 25 mg.
for motion sickness

The rectal thermometer & NEOPAP[®] SUPPRETTES[™]

(acetaminophen suppositories)



a rational
regimen for
childhood **fever**

NEW 5gr STRENGTH

Antipyretic for children

- No salicylate side effects
- Store without refrigeration
- Convenient rectal administration
- Available only by prescription
- Grooved for one-half suppository administration

Description: NEOPAP SUPPRETTES are available for rectal administration in potencies of 2 gr or 5 gr of acetaminophen in NEOCERA[®] Base (a unique blend of water-soluble Carbowaxes*).

Indications: For management of fever associated with common childhood infections.

Contraindications: Sensitivity to acetaminophen or the suppository base.

Warnings: Not for use in children under three years of age. Should not be administered repeatedly to patients with pulmonary, cardiac, renal, or hepatic disease.

Precautions: Prolonged administration may result in such withdrawal symptoms as restlessness and excitement when the drug is discontinued.

Adverse Reactions: No significant adverse reactions have been reported with NEOPAP (acetaminophen) SUPPRETTES. However, adverse reactions associated with administration (usually chronic) of this drug have included the following:

Blood: Cyanosis, methemoglobinemia, sulfhemoglobinemia, and hemolytic anemia; neutropenia, leukopenia, and pancytopenia.

Allergic: Skin eruptions, urticaria, fever.

Other: Hypoglycemia, CNS stimulation, jaundice.

Dosage and Administration: Children 3 to 6 years of age: One 2 gr suppository rectally 3 or 4 times daily; not to exceed 8 grains per day.
Children 6 to 12 years of age: One 5 gr suppository rectally 3 or 4 times daily; not to exceed 20 grains per day.

*Trademark Union Carbide.



Webcon Pharmaceutical Division
ALCON LABORATORIES, INC.
P.O. Box 1629
Fort Worth, Texas 76101

CLINICAL CONVENTION OF AMA

Portland, Oregon

November 30-December 5, 1974

Attending the Clinical Convention of AMA in Portland, November 30 to December 5, 1974, were Dr. Don Kilgore, our president; Dr. John Hawk, our senior delegate and Nancy, his wife; Dr. William Perry, our alternate delegate, and Ruth, his wife; Mr. Charles Johnson, our able Executive Director; Lib and I.

Meeting for a total of 16 hours 10 minutes, one-third of it devoted to AMA finances and related issues, the House acted on 77 reports and 68 resolutions for a total of 145 items of business.

Of the greatest concern to the delegates was the proposal by the Board of Trustees to increase annual dues for regular members, interns and residents, and medical students to \$200, \$35, \$25 respectively, effective January 1, 1975, and for the House to concur with the Board decision to discontinue advertising in AMA publications.

In addition, the Board of Trustees told the House of Delegates that two councils and eighteen committees of the board had been discontinued and recommended that the House of Delegates concur in its request that the House eliminate eleven of its committees. The Board also reduced the AMA staff, particularly the Field Staff.

From Report P of the Board of Trustees, statement by officers and discussion at the reference committee, the following is apparent:

—The AMA for all practical purposes is bankrupt, borrowing currently at the rate of \$1,000 per month.

Why did this happen? Whose fault is it?

The Board explains as follows:

The AMA, by inflation and recession, with underfinancing for a period of years,

was committed to "too much with too little." The optimal budget for 1975 to continue all programs at the best level was computed at \$42,502,089. To balance budget with expected income, this had to be reduced to \$35,258,129. This would mean no new programs in 1975 and further decrease in association liquid reserves if rate of inflation increased. Already capital assets have diminished or are committed in part to secure loans.

How did we get this way?

During the last 5 years substantial inflationary pressure and the need of AMA to expand its programs and activities in education, socio-economics, legislative and scientific activities have placed major demands on association resources. In 1970, the Board of Trustees requested that dues be increased from \$70 to \$150 annually. The House approved only \$110. There has been loss in operation of AMA in four of five years resulting in net reduction of reserves of \$6,676,000.

The Board states that in spite of stringent economics the projection for 1974 operation will result in an additional \$2.2 million deficit.

On October 21, 1974, AMA liquid reserves in terms of stock, cash and receivables were \$3.4 million. Part of this previously committed to secure loans. The need for additional borrowing may be required and the Board of Trustees authorized up to \$3 million in loans if necessary. Should this develop, the AMA would have to commit or liquidate capital (fixed) assets for continued operation.

The other AMA assets consist of fixed items such as Headquarters Building, furnishings and fixtures, three square blocks of adjoining properties which were purchased during the period 1961 to 1973.

These were purchased substantially with money other than membership dues. These represent a long-term investment of substantial value and should not be sacrificed at deflated value to meet operation deficit.

Thus, the board recommends a \$90 annual increase in dues to increase income, plus the reduction of councils and committees and the discontinuance of advertising in AMA publications, plus changes in the frequency of issue of certain publications.

The least understood, least accepted, and the subject of major discussion was the decision to discontinue nearly all advertising in AMA publications. The Board of Trustees states that their decision is based on both financial and ethical considerations.

In reviewing the financial status of publications, income from advertising is projected at \$9.5 million with a production cost of all publications amounting to around \$15 million. The pharmaceutical advertising dollar is stated as being unpredictable, not increasing at the rate of inflation. Competition for the advertising dollar is greater now. In the last three years there have been twelve new publications, each taking its share of the medical advertising market.

The Board feels that the AMA has been frequently and unjustly criticized as being biased toward pharmaceutical companies because it accepts drug advertising. While vehemently denying such bias they feel that the discontinuance of advertising will clearly establish the association's scientific and journalistic independence. Many took the decision as an effort to appease those who attack us, but this too was denied by the board.

It gradually developed that there was another termite in the woodwork and it may have more bearing on their decision than the above two. Since 1967 the AMA and the Internal Revenue Service have been discussing the matter of taxing advertising revenue. IRS saying that a gain

is realized and is therefore taxable. The AMA stand has been that this is a service to members and there is no gain realized. The final outcome of this is being delayed and has been extended (thus avoiding statute of limitations) on an annual basis since 1967 awaiting federal guidelines to be published setting forth the rules of determining the issue. Should the AMA lose and be committed to a large tax on all advertising retroactive to 1967 and since the outcome is indefinite, the Board of Trustees feels that the problem should not be compounded by continuing the advertising.

The House did not take well to this matter nor fully accept the explanation as given above. The House rejected the dues increase, but did impose a mandatory special assessment of \$60 for AMA members. They also called for a special committee of the House of Delegates to study the dues issue and report back at the 1975 annual meeting. By that time all of the facts, hopefully, will be made known to the membership, and the delegates will have an opportunity to study all of the options.

During the meeting the following awards were presented or authorized:

Benjamin Rush Bicentennial Award: Robert Parker, M. D., from Montgomery, Alabama, was awarded the Dr. Rodman E. Sheen and Thomas G. Sheen Benjamin Rush Bicentennial Award for Citizenship and Public Service. Presented by Dr. Malcolm C. Todd, AMA President, the award consists of a plaque and a \$5,000 honorarium.

Distinguished Service Award: William R. Willard, M.D., D.P.H., Moundville, Ala., Dean of the College of Community Health Sciences at the University of Alabama, was selected by the House as the recipient of the Distinguished Service Award. Dr. Willard's AMA award will be presented at the 1975 Annual Meeting.

Citation of a Layman: Harry Schwartz, Ph.D., Visiting Professor of Medical Economics at the Columbia University Col-

leges of Physicians and Surgeons on leave from the Editorial Board of the *New York Times*, was selected to receive the Layman's Citation for Distinguished Service. Dr. Schwartz, of Scarsdale, N. Y., is the author of *The Case for American Medicine*, a book published by David McKay Co. in 1972. His AMA award will be presented at the 1975 Annual Meeting.

Special Award for Distinguished Service: Ernest B. Howard, M.D., M.P.H., Executive Vice-President on leave from the AMA who will retire March 1, was given a Special Award for Distinguished Service by the House.

Dr. Howard, who joined the AMA in 1948 as Assistant General Manager, was given successive promotions until 1969, when he was named Executive Vice-President.

Commendation Resolution: Leo E. Brown, Assistant to the Executive Vice-President of the AMA, was presented with a Commendation Resolution for 24 years of service "to and for American medicine."

REPORT OF THE AMA PRESIDENT:

The price of defending medical freedom can be high, but that price must be paid, AMA President Malcolm C. Todd, M.D., told Delegates at the Clinical Convention in Portland.

Equating the "freedom that has made American medicine the most creative in the world" with the "very essence of professionalism cherished so highly by the nation's physicians," Dr. Todd pointed out that medicine's freedom, and hence its professionalism, are threatened.

Chief among the threats are various legislative proposals which would impose a compulsory national health insurance system and would make health care a public utility to "reduce each of us to the level of an electric wire or a telephone line," and manpower bills that would "imply indentured service in medical education."

Only a strong AMA can counter such threats and preserve professionalism, Dr.

Rondomycin[®]

(methacycline HCl)

CONTRAINDICATIONS. Hypersensitivity to any of the tetracyclines

WARNINGS. Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.** **Usage in pregnancy.** (See above **WARNINGS** about use during tooth development.)

Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in tibula growth rate observed in premature given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS. If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS. Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes, exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea. In uncomplicated gonorrhea, when penicillin is contraindicated, "Rondomycin" (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule: 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of "Rondomycin" (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia: 900 mg daily for six days.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

SUPPLIED: "Rondomycin" (methacycline HCl): 150 mg and 300 mg capsules; syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest POR information.

Rev. 6/73



WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512



**When the focus is on bronchitis due to
susceptible strains of *H. influenzae* and pneumococci***

Randomycin[®] 300 mg.
[methacycline HCl] Capsules

Delivers from the very first dose:

**studies show that after the first dose serum levels rapidly rise above
minimum *in vitro* inhibitory concentrations**

*Since many strains are known to be resistant, routine sensitivity testing is recommended.

The Role of the Detail Man

"I may be prejudiced, but I am very much in favor of the detail men I meet. Most of them are knowledgeable about the drugs they promote and can be a great help in acquainting me with new medication."

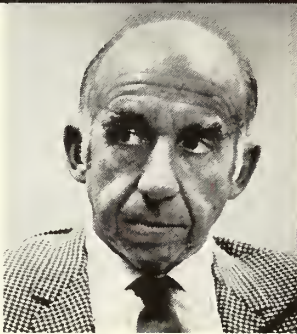
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.



Dr. Willard Gobbell
Family Physician
Encino, California

Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School



"In the total picture of dealing with health problems in this country, there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce — information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love — they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public — i.e., the patients — will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

*Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D. C. 20005*





Keeping things in balance...*

Antivert[®]/25 Tablets (25 mg. meclizine HCl)

***INDICATIONS.** Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation

has produced cleft palate in the offspring. Limited studies using doses of over 100 mg/kg/day in rabbits and 10 mg/kg/day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children. Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy. See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

ROERIG 
A division of Pfizer Pharmaceuticals
New York, New York 10017

Todd emphasized, but "it is impossible for its strength to be any greater than its finances."

Therefore, he issued a strong appeal to the House to support a \$90 dues increase, or, as an alternative, a special assessment.

While admitting that the AMA was not 100 per cent effective legislatively, he said that, "No element in society has a perfect score. Any element has to set its sights not on the best of all possible worlds, but the best of all possible realities."

He said that if the AMA is to be effective in seeking a National Health Insurance plan that would "respect both public needs and professional competence," in countering overly-stringent health planning and manpower bills, and in mitigating malpractice problems, then "it will need the money."

Dr. Todd said he personally believed that advertising does "play a useful role in physicians' education on drugs," but that "suspicion is easily planted and spread in these skeptical times, and there is reason to be sensitive to it." He urged careful consideration in the months ahead as to whether advertising should be banned from AMA publications.

In concluding his mid-term address, for which he received a standing ovation, Dr. Todd said:

"I leave you with two questions: Is the survival of our profession in danger? I say that it is. Is a dues increase the necessary price that we must pay for our survival? Again, I say yes. And it seems to me, by God, that no price could be so small for anything so great."

SUMMARY OF ACTIONS OF THE HOUSE OF DELEGATES: (as compiled by AMA staff)

Because of the wide-ranging nature of the actions taken by the House, and for the sake of clarity, this summary will be divided into five subject areas with appropriate sub-headings as follows:

A. Association and Internal Matters of the House

- B. Physicians and Hospitals and Medical Schools
- C. Physicians and the Government
- D. Physicians and the Public
- E. Miscellaneous

A. ASSOCIATION AND INTERNAL MATTERS OF THE HOUSE:

(1) *Housestaff Participation in AMA:* The Delegates adopted several recommendations designed to strengthen housestaff participation in the AMA.

They include: that the elected Executive Committee of the Intern and Resident Business Session assume advisory responsibilities of the Committee on Housestaff Affairs, which will be dissolved; that programs and priorities of the Department of Housestaff Affairs be developed annually by the department director and the chairman of the I & R Business Session, subject to review and approval of the Board of Trustees; and that responsibility for the editorial content of the Housestaff Newsletter and for the distribution of I & R Business Session reports be exercised by the Session's Executive Committee subject to appropriate approval and review in keeping with Association policies.

In a related action, the House approved an amended resolution calling for the development of model programs to involve medical students in the activities of organized medicine at all levels, and referred it to the Board and the Council on Constitution and Bylaws for implementation.

(2) *Professional Liability:* During a discussion of malpractice problems, the House adopted a recommendation calling for the Board to give "priority attention" to providing legal counsel and advice to AMA members and state societies in the event their professional liability insurance is not renewed.

The House also emphasized the necessity for state associations to seek legislative remedies for malpractice problems, and directed that the AMA continue to co-

The Upper Functional G.I. Disorder

The Pseudo-ulcer

Ulcer-like symptoms: no G.I. pathology



X-ray demonstrates normal stomach.

The patient is convinced he has an ulcer. However, symptoms are not quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient understand how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist.* Where milder cases may respond to counseling alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms.

In these cases, Librax as an adjunct can greatly contribute to the course of therapy. Its dual action can offer relief of both painful symptoms and excessive anxiety, because each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br. The antianxiety action of Librium® (chlordiazepoxide HCl) makes Librax exceptional among drugs for certain gastrointestinal disorders associated with excessive anxiety; the clidinium bromide (Quarzan™) component furnishes dependable antisecretory-antispasmodic action. Dosage is flexible; it may be adjusted according to your patient's requirements within the range of 1 or 2 capsules three or four times daily, up to 8 capsules daily in divided doses. Please consult the complete product information regarding precautions and adverse reactions.

*Rome HP, Brannick TL: Orientation and mechanism of functional disorders; clinicophysiology correlation, chap. 133, in *Gastroenterology*, edited by Bockus HL. Philadelphia, W.B. Saunders Company, 1965, p. 1116.

An adjunct in anxiety-related
upper functional G.I. disorders

Librax®

Each capsule contains 5 mg chlordiazepoxide HCl
and 2.5 mg clidinium Br.

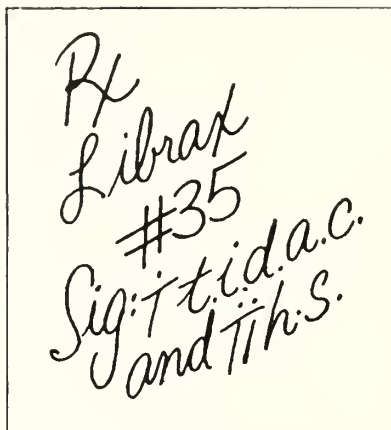
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Please see summary of product information on following page.

An adjunct in anxiety-related upper functional G.I. disorders

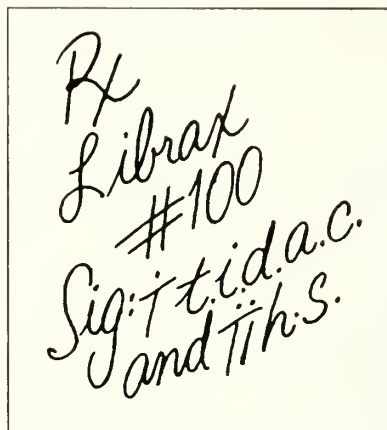
Librax®

Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.



Initial therapy

The initial prescription allows evaluation of patient response to therapy.



Follow-up therapy

Follow-up therapy with a prescription for 2 to 3 weeks' medication usually helps maintain patient gains.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures

necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anti-coagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

Dosage: Individualize for maximum beneficial effects. Usual maintenance dose is 1 or 2 capsules, 3 or 4 times a day, before meals and at bedtime. Geriatric patients—see Precautions.

How Supplied: Librax® Capsules, each containing 5 mg chlordiazepoxide hydrochloride (Librium®) and 2.5 mg clidinium bromide (QuarzanTM)—bottles of 100 and 500.



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operate with the Medical Liability Commission.

(3) *Clinical/Scientific Meetings Format Changed*: A separation of the fall business meetings of the House and the scientific meetings will be permitted beginning in 1977.

Under bylaws changes adopted by the House in Portland, the House will hold its fall meeting separately in cities recommended by the Board and selected by the House, and the scientific session will hold regional meetings at other times during the year as deemed necessary by the Board and at cities selected by the Board.

The new format was devised to allow regional scientific programming. The scientific assemblies will continue to be held in conjunction with Annual Meetings, however.

In other actions on internal matters, the House:

— Called for a definitive report at the 1975 annual meeting of AMA activities and programs related to PSRO.

— Rejected a Board of Trustees proposal to replace the Council on Legislation and many functions of the AMPAC Board of Directors with a new Council on Public Affairs.

— Referred a report on direct representation in the House of medical specialty societies back to the Council on Constitution and Bylaws for further consideration.

— And adopted a bylaws change permitting past Vice-Presidents of the AMA to become ex-officio members of the House (without voting privileges or reimbursement for meeting expenses).

B. PHYSICIANS AND HOSPITALS AND MEDICAL SCHOOLS:

(1) *Due Process*: The House adopted several recommendations which reaffirm the rights of all physicians, including housestaff and medical students, to due process. In related actions, the House adopted as AMA policy the proposition that a student's academic records should be open to inspection so that he/she may

profit educationally, and referred back to the Judicial Council for further study a report involving three cases of alleged violation of due process at the local level.

(2) *Guidelines for Housestaff Contracts*: The House adopted a set of revised guidelines for housestaff contracts. The proposed guidelines, as revised, had been approved by the Council on Medical Education, the Board of Trustees, and the Council on Medical Service.

(3) *Biomedical Research*: The House adopted a 10-point statement on biomedical research urging more federal funding with fewer restrictions. Prepared by the Board, the report sharply criticizes federal cuts in independent research grants and in the budgets of the National Institutes of Health.

The report urges that more unrestricted grants be awarded for research; that NIH be given more independence in establishing budget and research priorities; and that appropriations for biomedical research should be in proportion to their health-related spending.

(4) *Continuing Competence of Physicians*: Delegates also adopted a Board report calling for strong programs of continuing medical education and peer review as alternatives to relicensure since "the difficulties inherent in relicensure clearly outweigh any potential benefits."

Specific recommendations include all possible encouragement and support for the AMA, constituent societies, JCAH and other bodies in expanding CME programs; that the AMA give high priority to enhancing and reviewing effective methods of continuing competence; that patient satisfaction should be included in performance evaluation; and that well-designed peer review programs be endorsed as an important component of performance evaluation. The House also stressed that evaluation of performance, rather than knowledge per se, is the best method of appraising competence in patient care.

In other actions related to physicians and hospitals and medical schools, the

House:

— Adopted an amended resolution which urges that duplication of local peer review procedures be avoided; that medical audit or utilization protocols used in screening be limited to those which are demonstrated to be valid, reliable and which do not add needlessly to cost; and that when local peer review groups recognize that a hospital medical staff has adequate medical audit and utilization procedures, that fact should be recognized by governmental agencies and JCAH.

— Adopted a Board report detailing legally-approved methods for the exchange of information between and among medical societies and hospitals concerning a physician's hospital privileges or practice.

— And requested that a "comprehensive report" be presented at the 1975 Annual Meeting on questions and issues related to foreign medical graduates.

C. PHYSICIANS AND THE GOVERNMENT:

(1) *National Health Insurance:* Delegates gave the Board of Trustees a vote of confidence for its efforts to develop new approaches to NHI which maintain traditional AMA goals. The House adopted a Board report containing basic guidelines for NHI deliberations.

The guidelines include minimum federal involvement in the administration of any NHI program; state jurisdiction for licensure of physicians and regulation of insurance; no Social Security tax financing and administration of any program; funding through federal revenues, state revenues, and private funds including employer-employee contributions for private health insurance; comprehensive coverage for basic and catastrophic needs; and the maintenance of pluralism in health delivery.

(2) *Manpower and Planning Bills:* The House adopted an emergency resolution expressing unanimous opposition to U.S. House of Representatives bills which would divide the nation into health serv-

ice planning areas and treat health care as a public utility, and which would require medical students to reimburse the government for capitation.

The resolution was unanimously adopted on Wednesday, Dec. 4, and its substance presented to U.S. House Speaker Carl Albert and other Congressmen.

(3) *Prepaid Plans and Bonuses:* Delegates adopted a Judicial Council report which cautions that the payment of bonuses to physicians in prepaid health care plans such as HMO's for minimizing the utilization of services may interfere with the physician's obligations to his patients.

In other actions related to physicians and the government (and third parties), the House:

— Objected to language in insurance letters indicating the claims were "not medically necessary," since this encourages patients to decline to pay for services and is defamatory to physicians.

— Urged that Medicare intermediaries adhere strictly to regulations for reimbursement of chiropractors to those procedures defined in the regulations.

— Encouraged the acceptance and use by physicians of the AMA's Uniform Health Insurance Claim Form, and urged insurers to study the possible use of plastic "charge card" type identification cards for imprinting basic data on insurance forms.

— And urged the government to continue its present 55 m.p.h. speed limit for at least a one-year period, noting that traffic fatalities have declined 14.8% since the speed limit was imposed last year.

D. PHYSICIANS AND THE PUBLIC:

(1) *Weight Reduction Clinics:* The House took a strong policy position against the use of human chorionic gonadotropin for use in weight reduction. The House further resolved "that the AMA warn our citizens about the potential danger of such a weight control program." Clinics utilizing chorionic gonadotropin have

been established and widely advertised in various parts of the country.

(2) *Child Abuse*: The House adopted a substitute resolution encouraging state medical associations to survey child abuse laws in their states, and recommend more desirable legislation where necessary.

(3) *Health Care for Disadvantaged*: "Vigorous, high-priority" efforts to foster health care programs for disadvantaged segments of the population were recommended by the Delegates.

The reference committee report noted that the Council on Medical Service will continue to develop and implement long-range strategies to improve health care of the poor. The House requested regular reports of progress made.

(4) *Maternity and Newborn Care*: The House adopted two reports which reaffirm AMA policy to encourage insurance coverage of the newborn from the moment of birth, urge the health insurance industry to offer coverage for obstetrical care and any complications, and recommend that the insurance industry—as well as government—offer such coverage on the broadest possible basis.

In other actions relative to physicians and the public, the House:

—Supported state legislation to regulate the practice of acupuncture. The new policy says acupuncture should only be performed in research settings by a physician or under the direct supervision of a physician.

—Reaffirmed AMA endorsement of the fluoridation of water supplies.

—Adopted a Judicial Council report which holds that, "It is not unethical for a physician to authorize the listing of his name and practice in a (community) directory for professional or lay use which is intended to list all physicians in the community on a uniform and non-discriminatory basis. The listing shall not include any self-aggrandizing statement or qualitative judgment regarding the physician's skills or competence."

—Endorsed the right of a physician

to dispense ampicillin-probenecid for gonorrhea patients, reflecting a Judicial Council opinion that physicians have a duty to protect the confidentiality of patients who contract gonorrhea.

—And adopted a substitute resolution calling for the government to develop adequate safeguards for the transportation and storage of hazardous materials such as radioactive materials.

I have mixed emotions about writing this report to you. I deeply regret the resignation of Dr. Tom Parker and, I know, you will miss the eloquence of his writings and his dedication and devotion to duty. I am, however, honored by being permitted to serve in this position. I seek your counsel and direction and pledge to promote the best interest of our association as is expressed by the House of Delegates and Council of SCMA and, on matters undecided by these bodies, the majority opinion if it can be determined otherwise (by polls, society resolutions, specialty societies resolutions, etc.). This will determine my action. Foremost in my mind will be that I represent you, the members of the Association.

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SCMA Sets May 4-7 for Annual Meeting

The South Carolina Medical Association has set Sunday, May 4, through Wednesday, May 7, 1975, to hold its Annual Meeting in Myrtle Beach at the Landmark Motor Inn. Plans are being finalized now for the scientific and business sessions, and it is shaping up to be one of the finest meetings ever for the Association.

Dr. William H. Hunter, Speaker of the House of Delegates, urges all SCMA members to schedule this time on their busy calendars to take advantage of the educational value of outstanding speakers, and to enjoy the fellowship of their colleagues from around the state.

So that he may begin appointing Reference Committees, Dr. Hunter has asked all County Societies to submit to the Association the names of their delegates.

Also, Waitus O. Tanner, M.D., Chairman of Council, has asked that all Councilors submit an annual report of the activities in their areas. These should be written and prepared for inclusion in the House of Delegates Handbook. They must be received in the SCMA office no later than April 15.

Again planned for the meeting this year is the announcement of the Physician of the Year Award. County Societies should review their membership and select a physician who has proven his dedication not only to his profession, but also to his community. Nominations should be sent to the SCMA office by March 1.

SCMA is your association, and you need to support it with your attendance and your activities. The Annual Meeting is your best chance to get involved. Come learn what SCMA is doing for you.

PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

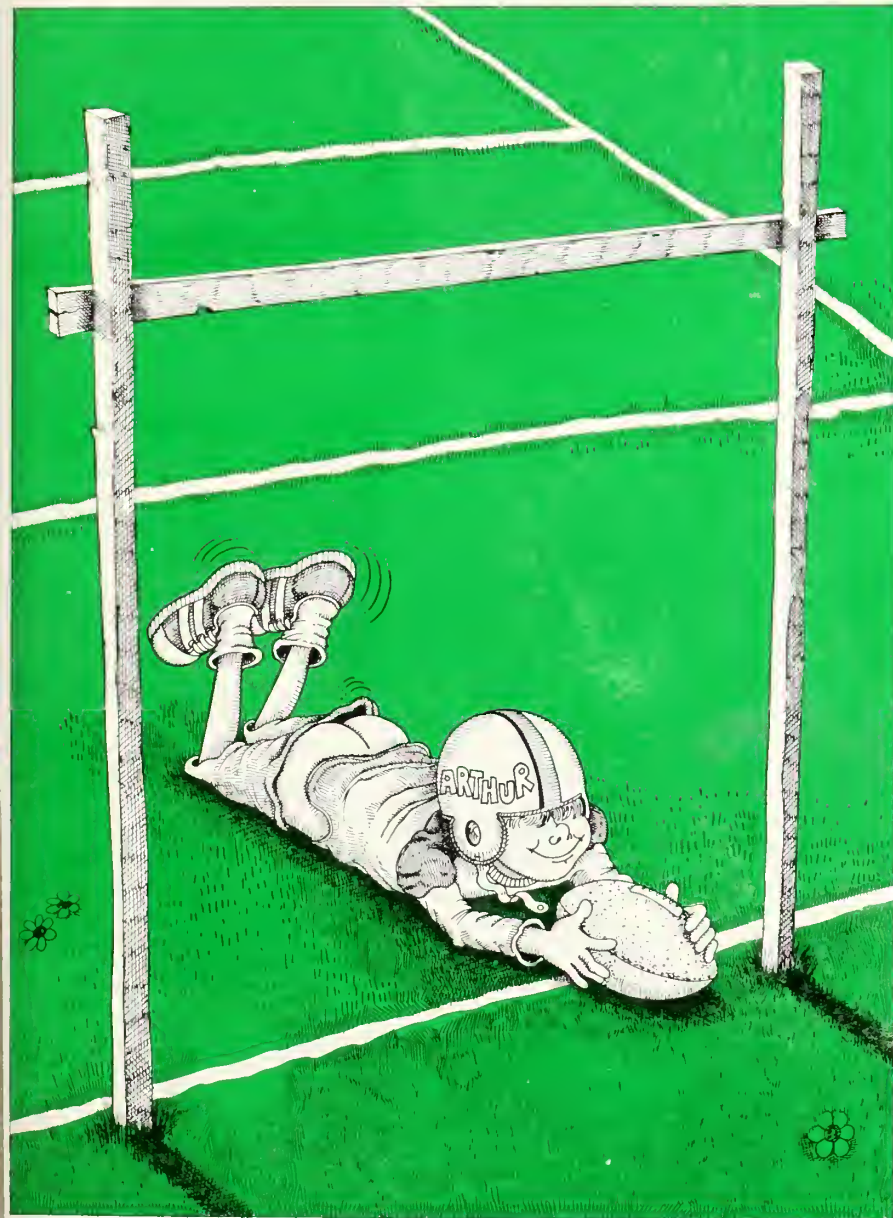
CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

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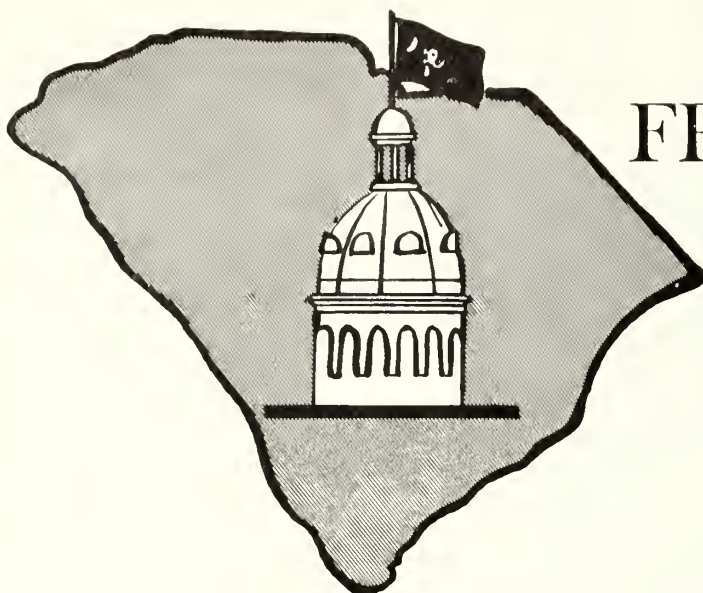
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ORAL SUSPENSION



FROM THE CAPITOL

RONALD B. HARRIS
DIRECTOR, LEGISLATIVE
AND PUBLIC AFFAIRS

The State's lawmakers are back at work, and the Capitol is buzzing with more legislators than ever before in the State's history. With the single member district plan, there are now 124 members of the House of Representatives. Of these, 42 are brand new to the legislative halls and 9 are returning after a hiatus.

The House is now comprised of 107 members who are Democrats and 17 who are Republicans. There are 13 blacks and seven women, a clear indication of the changing trend in elections.

The South Carolina Medical Association, under the direction of the Legislative Committee Chairman, Dexter B. Rogers, M. D., of Easley, has several legislative proposals this year. Dr. Rogers has mailed a copy of the legislative package to the officers of the county societies so they may inform all members of these proposals.

In all, SCMA plans to initiate more than a half dozen pieces of legislation this year, and will endorse many others of major importance to medicine. Professional liability is the most prominent of the proposals and will be in several phases including a form of peer discipline. Many states are in serious trouble over the availability of liability coverage, and the rates

for such insurance has become enormous. Through the proposed plans of legislation, SCMA hopes to ward off any further difficulties on this matter in the future.

Other programs SCMA wishes to initiate are: a bill to provide for confidentiality of medical information which is now in the hands of one of our ablest senators for introduction; a bill to protect doctors from liability suits when they inform the State Highway Department of a patient becoming medically unfit to drive; an amendment to allow acupuncture to be performed only in an accredited hospital under the auspices of research by the Medical University of South Carolina; and a bill or amendment to establish a South Carolina version of the Federal "Keough Act" to help private businessmen with their pension programs.

Members of SCMA will be kept informed of the status of bills important to medicine through the SCMA Newsletter. As it becomes necessary to solicit the aid of every member, a letter will be forwarded with explanation and suggestions. It will behoove every member of the association to contact his legislator and support SCMA-proposed legislation.

Many doctors will be contacted in the

very near future by Dr. Dexter Rogers and asked to volunteer to be the SCMA liaison with a senator or house member. Should you be contacted, please accept this important assignment. Favorable legislation is passed and unfavorable bills are defeated more often at the grass roots than in the Capitol lobby. Your legislative director can inform and urge, but you, the constituency, hold the power of persuasion.

In addition to the aforementioned bills SCMA will initiate, the association will support a bill to establish a Medical Examiners Commission; a bill to limit the terms of members of State commissions, committees and boards; and an amendment to the Nurse Practicing Act. Additionally, SCMA has gone on record supporting greater crime control.

Although the wheels of progress are running smoothly in the House of Representatives under the guidance of House Speaker Rex L. Carter, Democrat from Greenville, and the new Lieutenant Governor Brantley Harvey in the Senate, it will be some time before the new pieces of legislation will hit the floor. The Ethics Bill passed the Senate after considerable debate, but its House equivalent took several days longer. Now a compromise must be worked out between the two Chambers and this is expected also to be lengthy. To further increase the load, pre-filing has created an enormous load of bills which must be waded through, 307 to be exact.

DOCTOR OF THE DAY PROGRAM WELL ACCEPTED

Members of the Senate and the House of Representatives have expressed their appreciation to the South Carolina Medical Association for volunteering a doctor to be in the building during the times they are in session and much of the times dur-

ing committee meetings. So far, SCMA has supplied a doctor for every day, but there are several days in March, April and May which need volunteers. Please call or write the SCMA office and reserve the day (Tuesday, Wednesday or Thursday) you could serve. This is an excellent

way to increase the image of the medical profession in the eyes of our legislators.

The first day of the General Assembly was January 14. Since then the following doctors have served: Dr. Frank Martin, Columbia; Dr. C. Tucker Weston, Columbia; Dr. D. Strother Pope, Columbia (twice); Dr. D. Gavin Appleby, St. George; Dr. Harvey Bur-

nett, Columbia; Dr. Frederick W. Clemenz, West Columbia; Dr. Lucius Laffitte, Allendale; Dr. William Cantey, Columbia; and Dr. Thomas Parker, Greenville.

Also, Dr. Benton Burns, Sumter; Dr. Robert E. Jackson, Manning; Dr. Allen Jeter, Winnsboro; Dr. Hunter Rentz, Columbia; Dr. Halstead Stone, Chester; Dr. Al Cremer, Columbia; Dr. Michael Holmes, Kingstree; and Dr. Harry C. Taylor, Georgetown.

SENATE AND HOUSE COMMITTEES

Most of the work accomplished by the legislators at the State House is done in committee meetings. This part is seldom reported in the news media; consequently, its importance is sometimes minimized. Your legislative director is attending all committee meetings that are pertinent to the field of medicine and has established a good rapport with these chairmen and members. This has been accomplished because of the good reputation of South Carolina's physicians. As your representative we are striving to maintain that high degree of integrity. Your individual support is appreciated. Please contact me anytime this office can be of service.

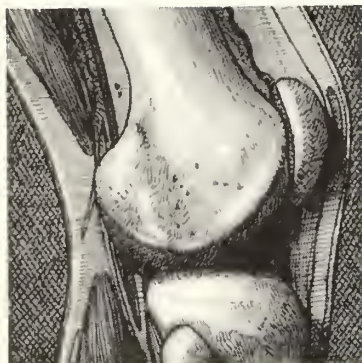
New Information Service Available From State House

As a part of the modernizing program at the State House, a computer system has been installed. Now any person may call toll free the number 1-800-922-1539 for the status of any Senate or House bill and other useful information. The Columbia number is 758-5870 for this service.

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| March 3-4 | Medicine I — George E. Burch, M.D. of Tulane University, Ernest Beutler, M.D. of the City of Hope National Medical Center, Duarte, Calif., Robert H. Williams, M.D. of the University of Washington Medical School, Arnold S. Relman, M.D. of the University of Pennsylvania Medical School, Howard M. Spiro, M.D. of Yale University, Edward W. Hook, M.D. of the University of Virginia, and Elam C. Toone, M.D. of the Medical College of Virginia in Richmond, Visiting Speakers. |
| March 13-14 | Medicine II — Eugene A. Stead, Jr., M.D. of Duke University, Visiting Speaker. |
| March 21 | Pharmacology — Leon I. Goldberg, M.D., Ph.D. of the University of Chicago and W. Leigh Thompson, Jr., M.D., Ph.D. of Case Western Reserve University, Visiting Speakers. |
| April 3-4 | Surgery — John H. Davis, M.D. of the University of Vermont, Visiting Speaker. |
| April 10-11 | Ophthalmology (Ninth Annual Residents Conference) — Paul Henkind, M.D., Ph.D. of the Montefiore Hospital and Medical Center, Bronx, N. Y., Herbert E. Kaufman, M.D. of the University of Florida, and Dan B. Jones, M.D. of Baylor College of Medicine, Houston, Visiting Speakers. |
| April 17-18 | Pathology — Thomas M. Peery, M.D. of George Washington University, Visiting Speaker. |
| April 24-25 | Obstetrics and Gynecology — Allen C. Barnes, M.D. of the Rockefeller Foundation, New York, Visiting Speaker. |

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Note: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in chronic and recurrent urinary tract infections.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia in elderly patients on diuretics, primarily thiazides. Sore throat, fever, pallor or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. Data are insufficient to recommend use in infants and children under 12.

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, allergy or bronchial asthma; and in those with glucose-6-phosphate dehydrogenase deficiency, where hemolysis may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus,

exfoliative dermatitis, anaphylactoid reactions, peri-orbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

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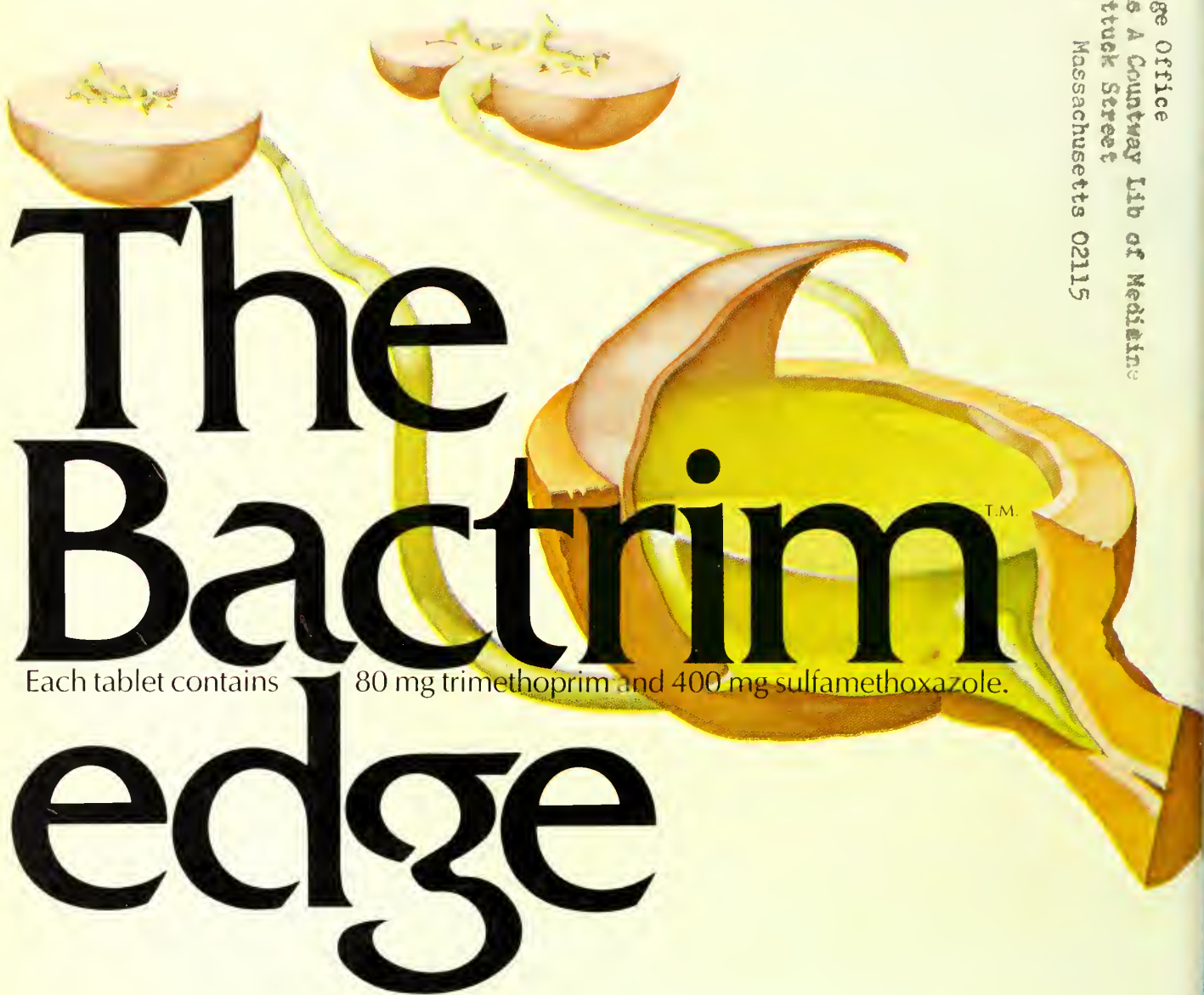
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MATERNAL DEATHS IN SOUTH CAROLINA 1961-1971

SELECTIVITY OF PROTEINURIA

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IMAGE—MUSC

VOLUME 71

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NUMBER 3

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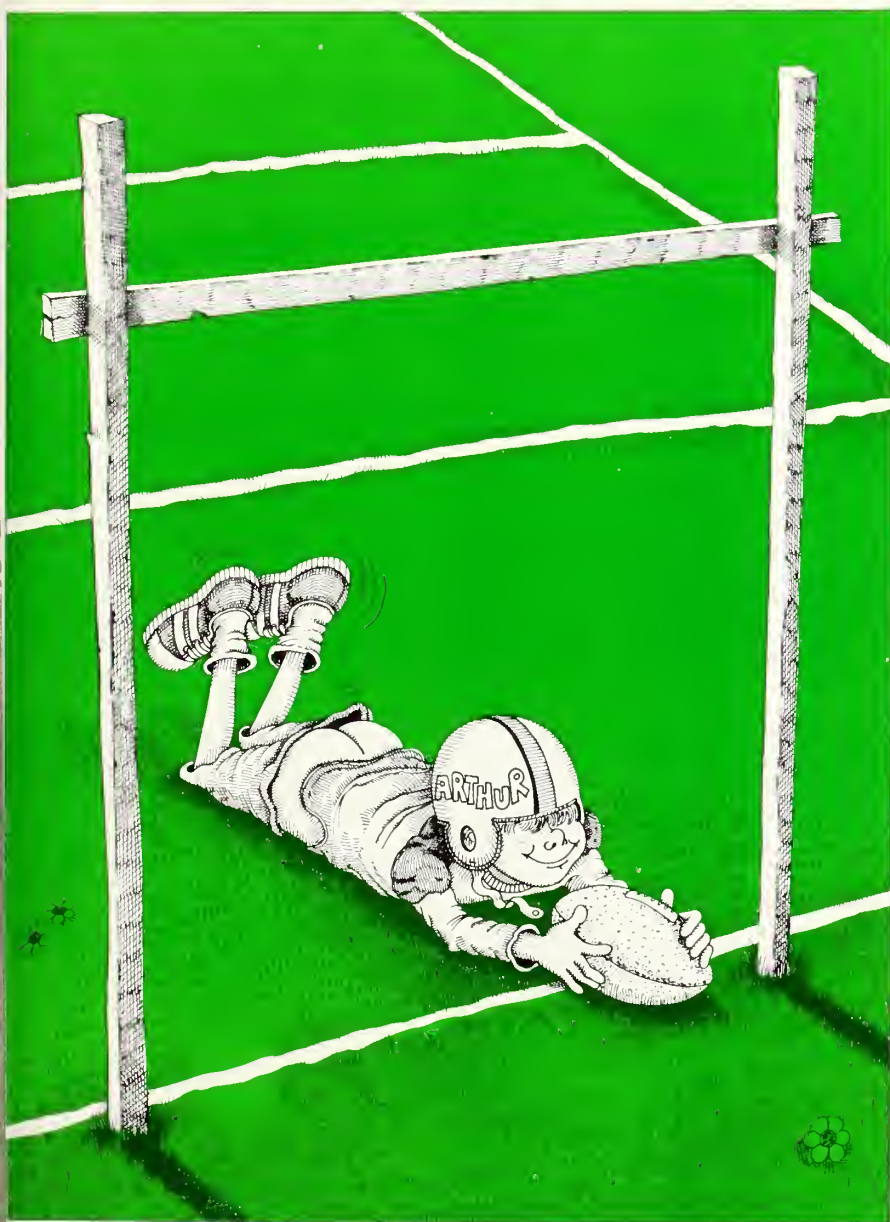
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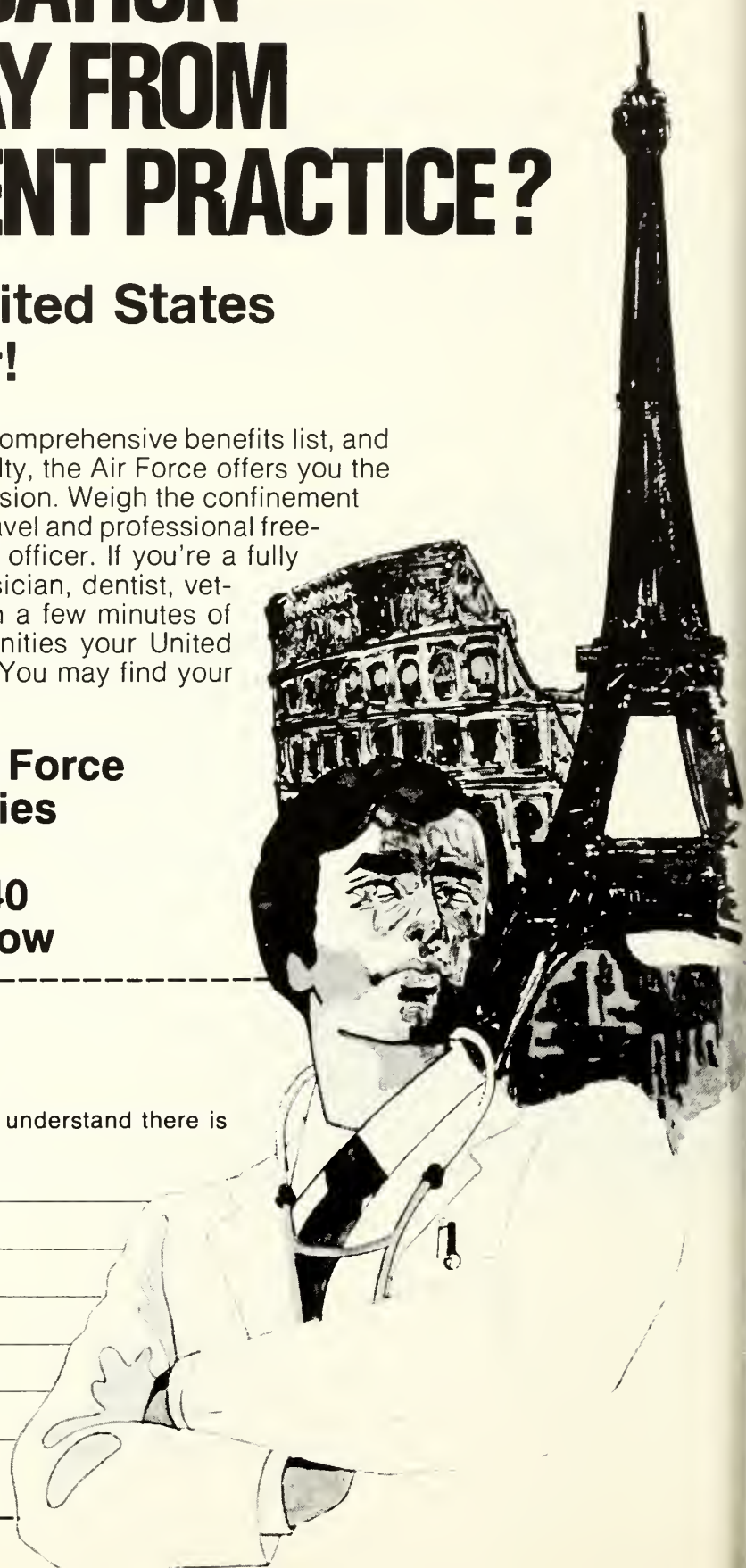
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SOUTH CAROLINA MEDICAL ASSOCIATION

VOLUME 71

MARCH, 1975

NUMBER 3

MATERNAL DEATHS IN SOUTH CAROLINA 1961-1971

JOHN G. EICHELBERGER, M.D.*
E. J. DENNIS, III, M.D.**

Maternal mortality figures are important because they reflect the adequacy of health care to women during their pregnancy, and by reviewing these statistics, we are able to improve obstetrical care in our State.

In 1935 there were 384 maternal deaths in South Carolina. This was the largest number of maternal deaths ever recorded in one year in South Carolina. In 1972 there were 16 maternal deaths and this was the smallest number of maternal deaths ever recorded in any one year in South Carolina.

This review is an informative and interesting look at the maternal deaths in South Carolina from 1961 - 1971 and is concluded with plans and constructive recommendations for the future obstetrical care in South Carolina.

Recently South Carolina adopted a new definition of maternal death. A maternal death is the death of a woman from any cause during pregnancy or within 42 days of termination of pregnancy irrespective of the duration of pregnancy at the time

of termination or the method by which it is terminated. (Effective January 1, 1973—old definition was 90 days).

The Maternal Mortality Committee in South Carolina was established in 1948 by the South Carolina Medical Association. The function is to review all maternal deaths in South Carolina in an effort to decrease maternal deaths in the State. Recent improvements in this Committee are:

- 1) The Committee now meets for all day scientific sessions two or three times yearly to review these deaths (instead of meetings six to seven times yearly for short sessions).

- 2) The Committee not only encourages the attendance of doctors that have the maternal deaths, but also an OB-GYN physician representative from each of the ten medical districts in South Carolina is asked to attend.

Some important factors that have contributed to the decrease maternal deaths over the years are:

- 1) Hospital care in the place of home delivery
- 2) Better trained physicians and nurses
- 3) Availability of more and better consultations
- 4) Better prenatal care

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MATERNAL DEATHS IN SOUTH CAROLINA 1961-1971

- 5) Availability of blood
- 6) Better obstetrical anesthesia
- 7) Safer obstetrical surgery
- 8) Proper use of drugs such as antibiotics and pitocin
- 9) More autopsies of maternal deaths
- 10) Education of the patient

- 11) Family Planning
- 12) Active Maternal Mortality Committee

The following tables represent some important statistics on maternal deaths in South Carolina from 1961-1971.

Table I

NUMBER OF LIVE BIRTHS RELATIVE TO MATERNAL DEATHS

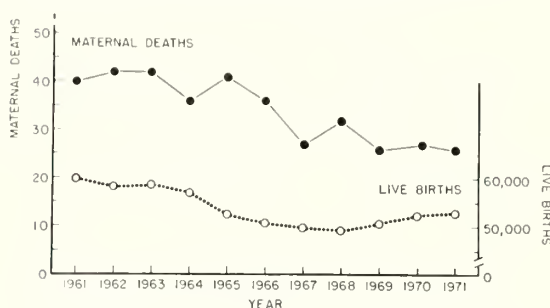


Table I shows the number of live births relative to maternal deaths. Both the number of live births and the number of maternal deaths have decreased but the percent of drop of maternal deaths is much greater. The percent of live births has dropped by 12 per cent and the percent of maternal deaths has dropped by 35 per cent from 1961 to 1971.

TABLE II

Leading Cause of Maternal Death

1961 — Hemorrhage	(17)
1962 — Toxemia	(9)
1963 — Toxemia	(15)
1964 — Hemorrhage	(11)
1965 — Hemorrhage	(9)
1966 — Hemorrhage	(12)
1967 — Hemorrhage	(9)
1968 — Hemorrhage	(7)
1969 — Sepsis	(8)
1970 — Sepsis	(12)
1971 — Sepsis	(7)

Table II shows the leading cause of maternal death in each year. The number in parentheses is the total number of deaths from the leading cause in each year. It is interesting to note that toxemia and

hemorrhage have given way to sepsis or infection in the last three years of the review.

Table III

AVERAGE AGE

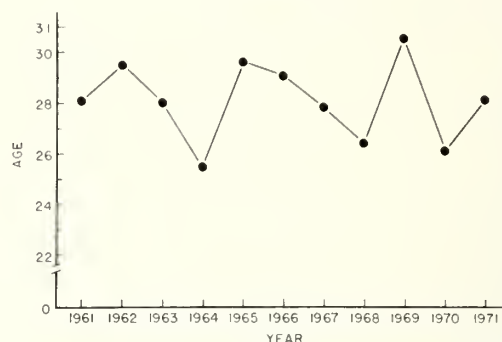


Table III shows the average age of maternal deaths in each year. The average has remained stable around age twenty-eight.

Table IV

RACE (Maternal Deaths)

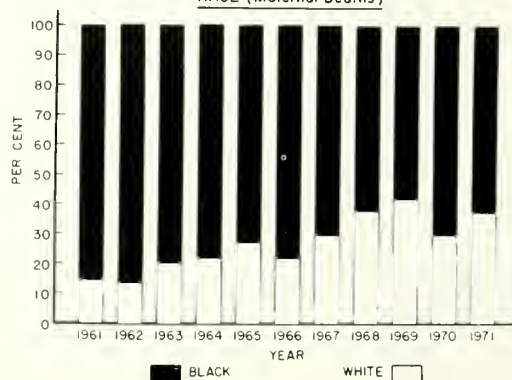


Table IV shows the maternal deaths by race. Although only approximately 40 per cent of live births are black, there are more black deaths than white. This percent has shown a trend towards a more equal distribution over the study period. The black is still definitely at a high risk.

MATERNAL DEATHS IN SOUTH CAROLINA 1961-1971

Table V

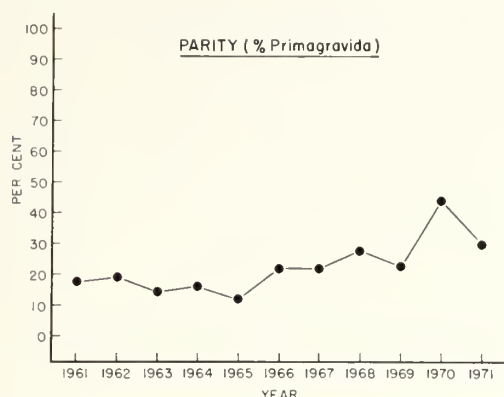


Table V shows the percent of maternal deaths that were primigravidas. There has been an increase in primigravida maternal deaths in the last two years of study, but this is probably best explained by the decreasing parity of the population due to increased availability and acceptance of sterilization and family planning.

Table VI

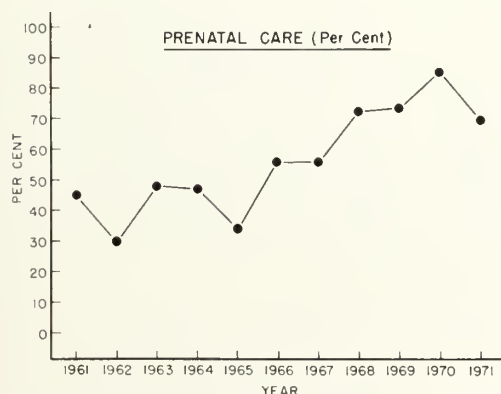


Table VI shows the frequency with which prenatal care was received by the patients who died during or soon after pregnancy. The incidence of prenatal care has shown an impressive rise from a low in 1962 of 30 per cent to a high in 1970 of 85 per cent.

Table VII

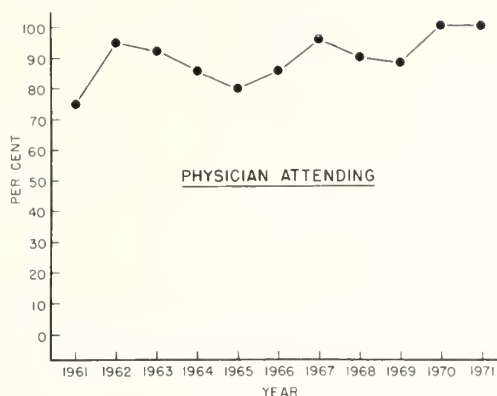


Table VII shows the maternal deaths that had a physician attending the patient at the time of delivery or at the time of death. This table shows an increase up to 100 per cent in 1970 and 1971.

Table VIII

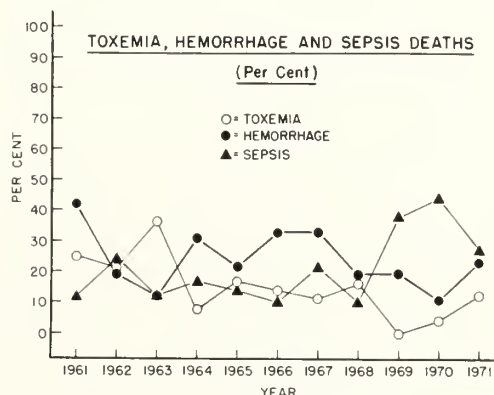


Table VIII compares the incidence of maternal deaths due to toxemia, hemorrhage and sepsis. The maternal deaths from toxemia have shown a dramatic decrease from 36 per cent in 1963 to a low of 0 per cent in 1969. The maternal deaths due to hemorrhage have shown a gradual decrease from a high of 43 per cent in 1961. Sepsis or infection as the cause of maternal deaths has shown a dramatic increase in the last three years of the study. The highest percentage was 44 per cent in 1970.

MATERNAL DEATHS IN SOUTH CAROLINA 1961-1971

Table IX

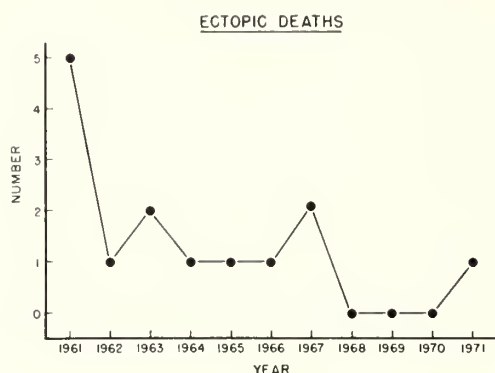


Table IX demonstrates the number of maternal deaths from ectopic pregnancies. Ectopic deaths are usually classified as hemorrhagic deaths.

Table XI

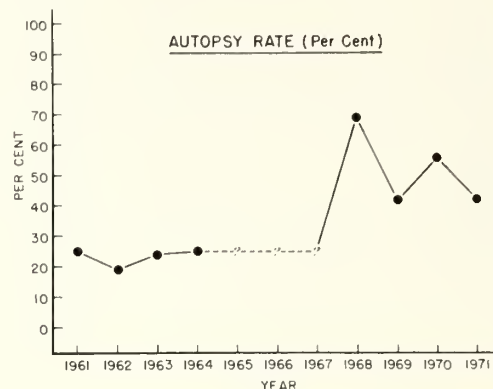


Table XI shows the autopsy rate in the maternal deaths. The autopsy rate has shown a very encouraging increase to a high in 1968 of 69 per cent.

Table X

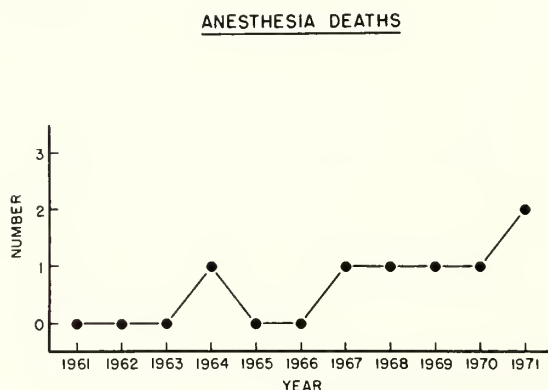


Table X shows the number of anesthetic deaths over the study period. Anesthesia deaths have shown an upward trend over the study period and these deaths have been related to both general and conduction anesthesia.

Table XII

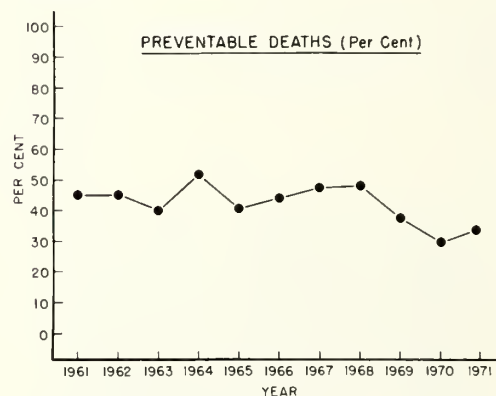


Table XII shows the percent of preventable deaths each year. The term preventable does not necessarily mean neglect on the part of the physician, but is used in the sense that under ideal conditions, better results would probably be obtained. There has been a decrease in the percent preventable deaths over the study period (down to a low of 30 per cent in 1970).

MATERNAL DEATHS IN SOUTH CAROLINA 1961-1971

Table XIII

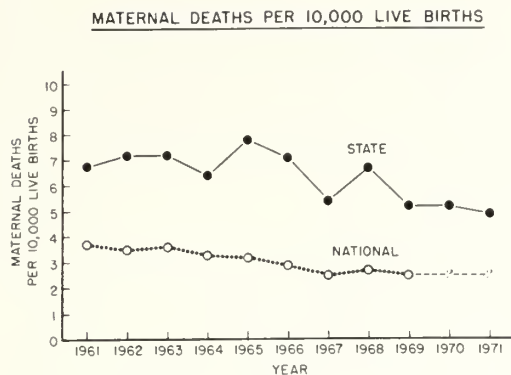


Table XIII compares the maternal deaths per 10,000 live births for South Carolina and for the Nation over the study period. Maternal deaths per 10,000 live births is the most commonly used figure to compare state to other states and to the National average. South Carolina continues to rank about two times the National average but we are definitely showing improvement.

In reviewing the maternal deaths in South Carolina during this period from 1961 to 1971, certain failures in obstetrical management are listed below:

- 1) Inadequate medical and surgical treatments of sepsis in pregnancy
- 2) Lack of proper, aggressive management of obstetrical hemorrhage
- 3) Improper use of drugs such as pito-cin
- 4) Inadequate management of ectopic pregnancy
- 5) Improper use of anesthesia
- 6) Inadequate recognition of abruptio placenta
- 7) Lack of recognition of impending eclampsia and inadequate early treatment
- 8) Continuation of pregnancy when therapeutic abortion indicated
- 9) Lack of recognition of non-obstetrical complications of the pregnant patient
- 10) Lack of educating the patient

In 1962, eighty-six per cent of deliveries in South Carolina were in the hospital and in 1971, ninety-five per cent were in the hospital.

TABLE XIV

TOTAL LIVE BIRTHS IN SOUTH CAROLINA HOSPITALS (1970)

Total Live Births	Number of Hospitals
1-499	34
500-999	16
1000-1999	10
2000+	4
	<hr/> 64

Total Hospitals in South Carolina performing Obstetrics

Table XIV shows the total live births in South Carolina hospitals in 1970. There are 64 hospitals in South Carolina that do obstetrics. Thirty-four hospitals (over one half) have fewer than 500 deliveries per year—that means less than 1.5 deliveries per day. It seems that a hospital would have a difficult time maintaining or even justifying the cost for a well-equipped and well-staffed delivery room if there are less than 1.5 deliveries per day.

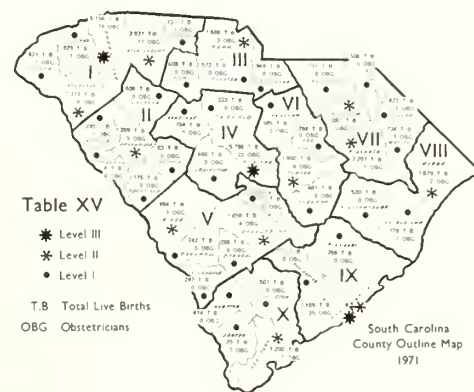


Table XV shows South Carolina divided up into ten medical districts and further divided into 46 counties. Each county shows the total number of live births and the number of obstetricians-gynecologists. Twenty-six of these 46 counties have no obstetrician-gynecologist.

There are proposals at the state level for obstetrics to be carried out at three different level hospitals. Some refer to these hospitals as Level I, Level II, and Level III hospitals,

MATERNAL DEATHS IN SOUTH CAROLINA 1961-1971

The Level III hospital is the regional or referral hospital and will number 3 or 4 in the state and have greater than 2,000 deliveries per year. The Level II hospital is the district hospital and at least one will be located in each medical district and will have greater than 1,000 deliveries per year. The Level I hospitals are the community hospitals which will have 500-1,000 deliveries per year. Many think that obstetrics should be discontinued at hospitals with less than 500 deliveries per year.

Based on the knowledge received from reviewing the maternal deaths for this study period, certain goals have been set forth for the future:

- 1) Prenatal care available to every pregnant patient
- 2) Every patient be delivered in the hospital
- 3) Every physician who does obstetrics should have well-equipped and well-staffed

delivery rooms and operating rooms in his hospital.

4) Every physician who does obstetrics should have consultation available from the major specialties, especially obstetrics.

5) High risk patients should be referred to obstetrician-gynecologist and preferable one at a district or regional hospital.

6) All Caesarean sections and complicated obstetrics should be done by the obstetrician-gynecologist.

7) Family planning be available post-partum.

8) Physicians support the Maternal Mortality Committee.

South Carolina has made some commendable gains in obstetrical care as demonstrated by this review. It appears also that obstetrical care can be further greatly improved in South Carolina. The physicians of the State should lead the way toward this improvement.

SELECTIVITY OF PROTEINURIA: ORIGIN OF THE PROTEINS AND POTENTIAL DIAGNOSTIC AID

KARL DOETSCH, M.S., M.P.H.*
RICHARD H. GADSDEN, Ph.D.*

AMOUNT OF NORMAL PROTEINURIA

The fact that every healthy person excretes a measurable and relatively constant amount of protein in the urine can no longer be questioned.¹⁻⁶ Many physicians, however, still regard urine as a protein-free fluid. This misconception has originated from traditional teaching and from misunderstood laboratory reports of routine urinalysis tests. The qualitative test for urinary protein is routinely reported as *negative* for practically all normal samples because the classical screening tests employed (e.g.: heat and acetic acid; sulfosalicylic acid; trichloroacetic acid; Albustix®) do not detect proteins at the low concentrations present. Even though great sensitivity can be demonstrated for pure solutions of albumin in physiological saline, the detection limits of these tests in the heterogeneous native urine samples are seldom lower than 25 mg/dl total protein. This observation is in accord with basic principles of precipitation analysis⁷⁻⁸ but generally has been overlooked by clinical analysts. It should be emphasized that these early tests were designed to detect primarily albumin, and that normal urine also contains a wide variety of other proteins.⁹ It is known that the screening tests are less sensitive to globulins and that mucoproteins are not detected at all.¹⁰ It is not surprising that the normal protein concentrations in urine that range from 3 to 25 mg/dl³ are not noticed. Because of the low concentrations and heterogeneity

of the protein species, and the large and varying amounts of interfering substances present in urine samples,¹¹⁻¹⁶ severe limitations of quantitative measurements have prevented the accurate determination of this clinical parameter. Indeed, there has been a great deal of controversy over exactly how much protein is normally excreted.¹⁷

Recent studies at the Medical University of South Carolina³ have indicated that twenty-four hour total urinary protein excretion ranges from 80 to 180 milligrams. Slight to moderate increases accompany physical or emotional stress.⁴⁻¹⁰ In most cases, however, increases greater than one hundred percent above the upper limit should not be expected. During the analysis of samples from eighty-eight apparently healthy adults, no protein excretion less than eighty-two milligrams per day was found. The finding that age or sex had no apparent effect on protein excretion is in accord with the literature.¹⁸⁻²⁰

SOURCES AND NATURE OF URINARY PROTEINS

Proteins appearing in the urine can originate from as many as six possible sources: 1) Plasma proteins passing through the glomerular membrane constitute $50 \pm 25\%$ of the normal proteinuria. Albumin is the predominant species. 2) Uromucoid and other mucoproteins synthesized on the outer surface of cells lining the renal and genitourinary tract^{6,18} comprise most of the remainder. The specific role of these proteins is not completely clear but they appear to function both in normal lubrication and in in-

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flammatory conditions. 3) Intracellular proteins liberated from kidney cells during normal turnover usually are not quantitatively significant, but may be selectively identified in conditions of increased activity such as carcinomas. 4) Foreign proteins appearing in the urine because of the presence and destruction of microorganisms may become quantitatively significant in progressive infectious processes. 5) Lipoproteins and unusually high molecular weight globulins may be present in rare cases involving lymphatic drainage into the urinary tract. 6) Proteins of an unusual nature but not exceeding the size of albumin may be present in certain pathological conditions demonstrating dysproteinemia. An example is the immunoglobulin light chains, also known as Bence-Jones protein. Breakdown of erythrocytes or leukocytes, or presence of prostatic (or seminal) fluid or intestinal conduits could also contribute to total urinary protein.

Both physiological and pathological alterations can result in elevated urinary protein excretion patterns arising from one or more of the aforementioned sources. Increases in plasma proteins result from tubular damage and/or increased glomerular permeability. Certain inflammatory conditions may result in elevated amounts of mucoprotein while increased rates of tissue destruction would result in more proteins of intracellular origin. Microbial infections result in the presence of foreign protein species. Although lymphatic fistulas occur only rarely, a variety of atypical proteins may appear in the urine of patients with dysproteinemias. Great diversity of protein species found in the urine is therefore possible and causes a variety of problems in analysis. Most protein methods have relied on determination of elemental nitrogen or of certain functional groups measured relative to gravimetric analysis.¹¹ Modern technological advances such as disc gel electrophoresis, and immunochemical methods including radioimmunoassay now make it possible to attain greater sensitivity and specificity. It is therefore possible to determine the selectivity of pro-

teinuria to aid in the more specific diagnosis of renal disorders.

RENAL PROTEIN PHYSIOLOGY

The kidney has been overlooked as an important site of protein metabolism. It has been reported that 10 to 15% of normal catabolism of albumin occurs in the proximal tubular cells.⁶ This amounts to almost two grams per day. Albumin and smaller plasma proteins are filtered through the glomerular membrane with efficiency inversely related to their size, except that larger plasma proteins are almost entirely excluded in the absence of glomerular membrane damage. Ninety-nine percent of the protein is reabsorbed from the glomerular filtrate in the proximal tubules by the non-specific mechanism of pinocytosis.⁵ The efficiency of reabsorption is again inversely related to the size of the protein. For example, plasma lysozyme (MW 15,000) is completely reabsorbed.⁴ From 180 liters of glomerular filtrate produced daily, 4 to 15 grams of plasma protein are generally reabsorbed. Protein concentration in the glomerular fluid therefore must be 20 to 85 milligrams per liter, or somewhat less than in cerebrospinal fluid. This approaches 0.1% of the plasma protein concentration. The low normal renal threshold for protein reabsorption is believed to be altered slightly when protein concentrations of the glomerular filtrate are increased so that greater amounts are reabsorbed and catabolized.⁵ The excessive spillover directly results in elevated protein excretion. The greatest portion of the excreted protein most often is albumin, and for this reason the earlier methods of protein assay designed to most effectively determine albumin have been useful to monitor large changes in protein excretion. Normal amounts of protein, however, were not determined with reliability.

Speculation over the catabolic fate of reabsorbed protein is a matter of controversy. There is evidence that the ingested protein endocytosis vacuoles fuse with tubular lysosomes containing proteases and are thereby hydrolyzed to constituent amino acids. These are in part used locally

for new protein synthesis and in part returned to the blood plasma by the regular transport mechanisms.⁵ Other evidence suggests the transport of intact proteins via exocytosis to the lymph system and then to the blood by way of the thoracic duct, or even directly by exocytosis from the tubular cells to the blood.^{4,6} The actual physiological fate of protein entering the proximal tubules is likely a combination of these proposed mechanisms. It seems reasonable that perhaps half of the protein (probably a significant portion of the larger species including albumin) returns to the blood via the lymphatics, while much of the remaining returns directly to the blood (most likely the smaller species), and some is catabolized to amino acids in the lysosomes (both large and small species).

CLINICAL SIGNIFICANCE OF PROTEINURIA

Physiologic factors. It has been shown that as much as a six-fold increase of protein excretion can occur during heavy physical exercise. The proteins are almost entirely of plasma origin and suggest that a change in glomerular permeability occurs. Poortmans has proposed that constriction of the afferent arterioles resulting from increased blood epinephrine levels slows renal plasma flow and consequently the glomerular filtrations rate.⁴ This would permit a greater diffusion of protein into Bowman's Capsule. When plasma flow returns to normal, the excessive protein would be washed through the system and appear in the urine. Others have proposed that decreased renal plasma flow in the peritubular capillaries could decrease the reabsorption threshold.⁴

A twelve-fold increase in protein excretion upon standing compared to the recumbent position has been observed in a condition termed "postural proteinuria." Even larger increases have been found in "orthostatic proteinuria." These conditions apparently are benign and the physiological mechanisms have not yet been elucidated.⁴

Elevated concentrations of plasma proteins (MW < 69,000) can result in pre-

renal proteinuria. The proteins pass through the glomerular membrane and are not effectively reabsorbed in the proximal tubule. For example, albuminuria has been demonstrated in cases where plasma concentration of albumin was raised by infusion.⁴ Upon saturation of plasma haptoglobin, free hemoglobin from plasma enters the glomerular filtrate and appears in the urine. Myoglobin is found following traumatic insult, and in multiple myeloma the light chains of immunoglobulins (MW 22,000 or 44,000) are usually present. Minute amounts of this Bence-Jones protein are normally present in urine but go undetected.⁴

Increased glomerular permeability result from a variety of conditions ranging from microbial infections to autoimmune diseases. Protein loss may exceed twenty grams per day.⁴ Almost any protein above the usual amount in the glomerular filtrate is excreted because of the low threshold for protein reabsorption. Impaired function of the proximal tubule may result in decreased reabsorption of protein. Proteinuria, however, rarely exceeds two grams per day.⁴ Piscator²¹ first documented an unusual pattern of proteinuria in factory workers chronically exposed to cadmium dust that resulted in selective impairment of proximal tubular function with no effect on glomerular permeability. Other conditions were later found associated with similar proteinuria patterns. These included analgesic abuse, vitamin D intoxication, hypokalemia, galactosemia, Fanconi syndrome, and various other conditions demonstrating a healthy glomerular membrane in the presence of tubular necrosis.²⁰

Accurate evaluation of the nature of proteinuria could be valuable as a diagnostic aid in evaluating kidney disease. Selectivity of proteinuria can be demonstrated when tubular impairment is present in the absence of glomerular damage, or in the reverse situation where glomerular damage is present in the absence of tubular impairment. In the latter situation, degree of proteinuria is generally greater; the urinary proteins are com-

SELECTIVITY OF PROTEINURIA

prised of albumin and larger plasma proteins with the remarkable absence of smaller proteins. In the former situation, degree of proteinuria is milder; the urinary proteins are comprised of albumin and smaller plasma proteins with the remarkable absence of larger proteins. These phenomena are easily explained by the physiological process of filtration/reabsorption of the spectrum of plasma proteins. Usually proteins larger than albumin are not filtered while the smaller proteins are almost completely reabsorbed.

In determining selectivity of proteinuria, diagnostic tests need not be limited to those that can specifically identify proteins. Diagnostic enzymology can indicate the relative sizes of urinary proteins.^{22,23} For example, if tubular damage exists, there is an accompanying increase in lysozyme (MW 15,000) activity. If glomerular damage exists, there is an accompanying increase in activity of lactate dehydrogenase (MW 140,000) from plasma. There are specific increases or decreases of urinary enzyme activities in a variety of clinical conditions, e.g. carcinomas of various loci (intra- or extra-renal) and in the prediction of renal transplant rejection crises.^{23,24} Actual clinical usefulness of urine enzymology has been in a state of controversy because of technical problems resulting in unreliable assays. But these problems can be overcome through application of recently devised technologies and materials^{25,26} that lend themselves to clinical laboratory situations.

It should be emphasized that total urinary protein excretion is still the most sensitive indicator of renal disease.^{19,20} Diagnostic value of the determination of selectivity of proteinuria by protein methods and urine enzymology will increase as experience is gained and reliable interpretation of laboratory data results.

METHODOLOGICAL CONSIDERATIONS

Determination of Proteinuria. The use of earlier methods such as the one of

Foster et al.²⁷ suffers from specific shortcomings³ and needs to give way to modern analytical technology. Comparison of patient disc gel electrophoresis patterns to normals and to known controls²⁸ and the use of recently developed immunochemical methods of analysis employing nephelometry, immunoelectrophoresis and radioimmunoassay²⁹⁻³² can be used to specifically quantitate the protein species. In gel filtration methods,^{3,33} the reagents can be varied to employ different molecular size exclusion limits in order to give additional information about the nature of the proteins present.

Determination of enzymuria. From the observed selectivity of urinary protein patterns, it follows there must exist a selectivity of enzyme patterns. Physicians have requested laboratory aid through use of diagnostic urine enzymology for differential evaluation of renal diseases and of early stages of renal allograft rejections,³⁴ but attempts have been disappointing and controversial.³⁵⁻³⁷ The most important reason for conflicting results and interpretations has been the lack of a completely suitable method for gently and efficiently isolating the enzymes from the variety of substances present in human urine. These substances can erroneously affect enzymatic assays by inhibiting or enhancing activities.³⁸ It is not surprising that dialysis is neither effective nor practical for processing large numbers of samples encountered in clinical laboratories.²⁵ The interference removal problem of analytical methodology is not without solution, however, and there is great potential in this area of diagnostic laboratory medicine. There is a little doubt that with time a battery of urinary enzyme tests will be offered in a manner analogous to the currently popular batteries of serum enzyme tests.

Determination of selectivity of proteinuria should prove to be a new aid in clinical diagnosis and management of patients with renal disorders.

SELECTIVITY OF PROTEINURIA

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GASTROJEJUNOCUTANEOUS FISTULA AND "ELEMENTAL" ALIMENTATION

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Feared and respected by surgeons are complications that can occur after a Billroth II gastrectomy. The seriousness of a major gastrojejunal anastomotic leak carries a well documented high mortality.¹ Support of nutrition in such cases has been emphasized as most vital.² Until recently, wasting was the rule, but this is not necessarily so with present methods of alimentation. The chemically defined elemental diet (Vivonex, standard) as outlined by Bury *et al*³ was used so successfully in the case herein described that it was considered worth reporting.

CASE REPORT

H.C., a 51-year-old diabetic alcoholic, was admitted with major upper gastrointestinal bleeding on 10-17-73. By history he had bled previously from a duodenal ulcer. On 10-23-73 a Hofmeister type Billroth II hemigastrectomy was performed. The lesser curvature of the antrum was indurated and fixed to a firm inflamed pancreas. The resected specimen revealed benign superficial ulceration along the lesser curvature. Vagotomy was not performed. On 10-28-73 he bled again. Fibre-endoscopy on 10-31-73 revealed no varices or proximal erosive gastritis. Old clot obscured the gastrojejunal area. After twelve postoperative transfusions, he was returned to the operating room on 11-2-73 and a higher gastric resection performed along with the creation of a catheter jejunostomy. There was no further bleeding. The resected specimen revealed superficial ulceration of the stomach adjacent to the gastrojejunostomy.

On 11-8-73 he drained copious amounts of bile, gas, pus and gastric content through the abdominal incision. Sump suction in the fistula was started. The presence of small bowel function allowed elemental alimentation (Vivonex, standard) to be given by jejunostomy tube in a continuous drip. The amount was gradually increased until twelve packs (3600 calories) were

given daily in 3000cc of water. Intravenous fluids replaced the measured sump output.

A gastrograffin study on 11-14-73 (Figure 1) outlined the gastrojejuno cutaneous fistula. Repeat studies on 11-29-73 (Figure 2), 12-10-73 (Figure 3) and 12-20-73 (Figure 4) revealed progressive closure of the fistula. There was no diarrhea during the administration of Vivonex into the jejunum. On two occasions a blenderized liquid diet was tried but cramps and diarrhea resulted. This was immediately corrected by substituting the Vivonex feedings. Jejunal tube Vivonex was discontinued on 12-20-73 and oral intake was started.

The patient was discharged on 1-11-74. In follow-up on 3-26-74, he was doing well except for Tiron suture sinuses in the abdominal wall.



Fig. 1. Nov. 14, 1973.
The fistulous cavity is well outlined.

DISCUSSION

Gastrojejunal anastomotic leak is often fatal: eleven out of thirteen, Edwards *et al*¹ and two out of four, Miller and Dorn.⁴ Diversionary surgery was successful in one of two cases reported by Rosenberg.⁵

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Fig. 2. Nov. 29, 1973.
Fistulous cavity still well visualized.



Fig. 3. Dec. 4, 1973.
Fistulous cavity no longer visible.

Wolfe showed that elemental alimentation compares favorably with the intravenous hyperalimentation in experimental low intestinal fistula at terminal ileal level.⁶ With the fistula at proximal jejunal level, however, intravenous hyperalimentation was markedly superior. Had it not been for the feeding jejunostomy tube distal to the fistula in this case report, intravenous hyperalimentation would have been necessary.

SUMMARY

A case of continued gastric hemorrhage after an Hofmeister type Billroth II hemigastrectomy necessitated a second high subtotal gastrectomy. A gastrojejuno-cutaneous fistula then developed, causing marked gastric and biliary drainage. Serial radiologic studies demonstrated rapid healing of this fistula. Such a good result is attributed to the elemental nutrition which was so well tolerated by jejunostomy tube.



Fig. 4. Dec. 20, 1973.
The anastomosis is functioning normally.

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PROPRANOLOL: ANOTHER VIEW

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After reading the Clinical Report by Dr's Wallace and Wilson, we were concerned that in their preoperative use of propranolol the possible effects upon the patient's anesthetic course were not considered. Often preoperative techniques and drugs are employed without considering possible interactions with other drugs or procedures. In the past, examples of this type of abuse have included anti-hypertensive medications, phenothiazines, and M.A.O. inhibitors. More recently, Levo Dopa and now propranolol have entered the picture.

A majority of patients with hyperthyroidism can be controlled and prepared preoperatively with the classical antithyroid drugs and iodine. For the occasional patient who fails to respond to this regime, or for the patient who may be allergic to the antithyroid drugs, the use of a beta blocking agent such as propranolol should be considered. However, because preoperative treatment with propranolol is an easier and less time consuming method, there may be physicians who will attempt to treat all of their hyperthyroid patients with this drug before proper evaluation of the technique is made.

Propranolol is a potentially dangerous drug whose interaction with anesthetic agents must be considered. Propranolol, besides being a beta one and beta two

competative blocker, has a local anesthetic effect on membrane events in myocardial cells, and thus effects myocardial conduction and performance. In the hyperthyroid patient, acute thyroxin levels are unaffected by beta blockade. Thus the increase in oxygen consumption associated with hyperthyroidism is left unabated, while the body's ability to increase oxygen delivery is impaired. When another direct myocardial depressant, such as any general anesthetic, is added to the situation of increased oxygen consumption and local anesthetic affect of propranolol upon the myocardium, hypotension and hypoxemia become real possibilities. If, in addition, the patient should have preexisting cardiac disease, such as compensated congestive heart failure, hypertension with left ventricular hypertrophy, or coronary artery disease, a catastrophe may be in the making.

Proponents of propranolol will point out that it has a half life of only four hours, and theoretically its blockade can be overdriven by the administration of Isoproterenol. However, depending upon the dose of the drug, traces of propranolol or its metabolites have been found in tissue for as long as twenty-four to thirty-six hours post administration. Circulatory depression for more than just several hours is a distinct possibility.

In the face of acute circulatory depression secondary to beta blockade, the following regime has been advocated (Table 1):

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Table 1. Treatment of circulatory depression in the presence of Beta Blockade

- A. Competative antagonism with Isoproterenol
- B. Anti-cholinergic drug (atropine) to relieve the bradycardia secondary to unopposed parasympathetic input
- C. Drugs which act by other than beta pathways:
 - 1. Digitalis
 - 2. Calcium
 - 3. Glucagon
- D. Paradoxically, epinephrine has been effective when Iso-proterenol failed


SUMMARY

There is no doubt that in the occasional patient the use of propranolol may be justified in order to reduce the occurrence of thyroid storm. However, there is no place for tunnel vision in an interdisciplinary approach to patient care.

Carefully controlled studies evaluating this new therapy should be performed. The potentially dangerous interaction of propranolol with commonly used anesthetic agents should be a consideration in these studies.

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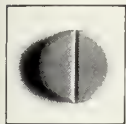
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A black and white photograph of three children on a wooden structure, possibly a playhouse or a set of stairs. One child is sitting on a ledge in the foreground, looking towards the camera. Two other children are positioned higher up on the structure, one looking out from a window-like opening and the other standing on a platform. The image has a grainy, high-contrast quality.

Ortho announces
a unique,
broad-spectrum
anthelmintic
effective against
whipworm...

new
Vermox^{TRADEMARK} chewable
(mebendazole) tablets

...and highly effective against roundworm, hookworm and pinworm in single or mixed infections



No dosage calculations — one simplified dosage,
regardless of weight or age[†]

whipworm, roundworm, hookworm and mixed infections:

1 chewable tablet b.i.d. for 3 consecutive days

pinworm: 1 chewable tablet

If the patient is not cured three weeks after treatment, a second course of treatment is advised.

highly effective

	Mean cure rates	Mean egg reduction
Whipworm	68%	93%
Roundworm	98%	99.7%
Hookworm	96%	99.9%
Pinworm	95%	— — —

simplicity of administration

patients can take the tablet at any time.
It can be chewed, swallowed or crushed and mixed with food. No messy liquids to pour.

not a dye

new Vermox* (mebendazole) chewable tablets will not stain clothes, teeth, feces, toilet bowls, etc.

convenient

neither laxatives nor special diet required. Therapy does not interfere with daily activities.

well tolerated

transient symptoms of abdominal pain and diarrhea have occurred
in cases of massive infection and expulsion of worms.

[†]Vermox has not been extensively studied in children under 2 years of age, and thus, the relative benefit/risk should be considered before treating these children. Vermox is contraindicated in pregnant women. (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Indications Vermox* (mebendazole) is indicated for the treatment of *Trichuris trichiura* (whipworm), *Enterobius vermicularis* (pinworm), *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed infections.

Efficacy varies in function of such factors as pre-existing diarrhea and gastrointestinal transit time, degree of infection and helminth strains. Efficacy rates derived from various studies are shown in the table below:

	Trichuris	Ascaris	Hookworm	Pinworm
cure rates mean (range)	68% (61-75%)	98% (91-100%)	96% —	95% (90-100%)
egg reduction mean (range)	93% (70-99%)	99.7% (99.5-100%)	99.9% —	— —

Contraindications Vermox is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

*TRADEMARK

Precautions **PREGNANCY:** Vermox has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since Vermox may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and administration The same dosage schedule applies to children and adults.

For control of trichuriasis, ascariasis, and hookworm infection, one tablet of Vermox is administered morning and evening on three consecutive days. For control of enterobiasis, a single tablet of Vermox is given.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

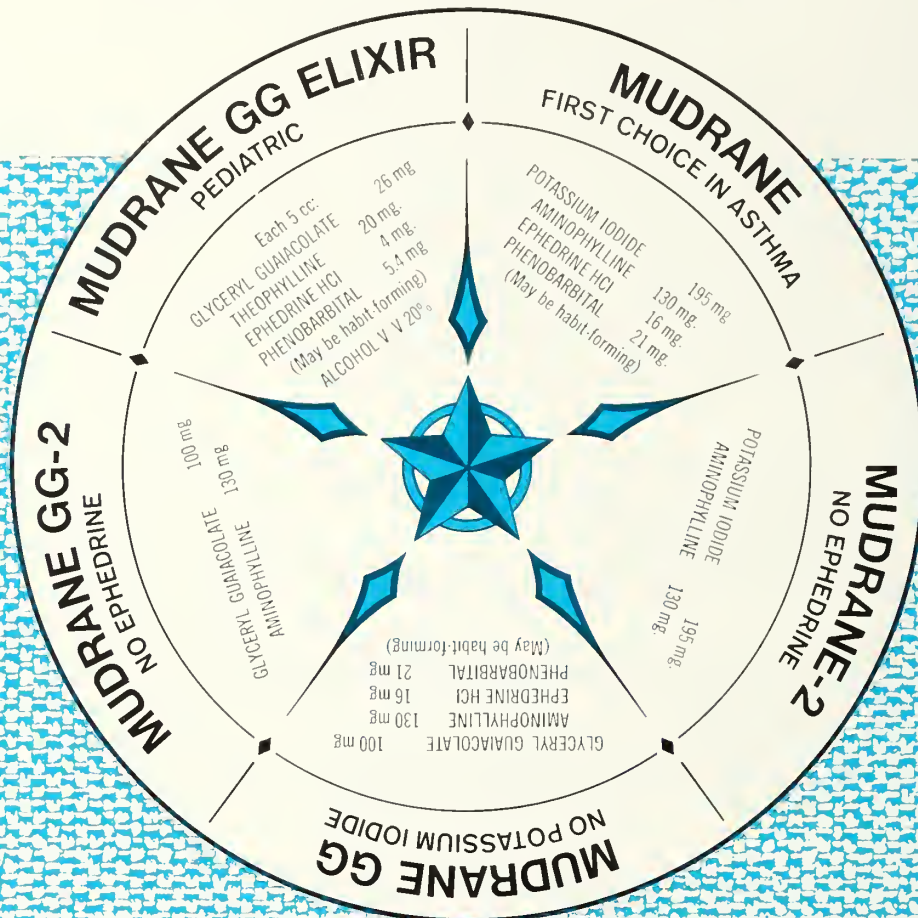
How supplied Vermox is available as tablets, each containing 100 mg of mebendazole, and is supplied in boxes of twelve tablets.

Ortho Pharmaceutical Corporation,
Raritan, New Jersey 08869



The MUDRANES

Discreet formulations of four well regarded drugs for the relief of bronchial distress—Potassium Iodide, Glyceryl Guaiacolate, Aminophylline, Ephedrine with Phenobarbital (to lessen cardiac stimulation).



INDICATIONS: For the prompt symptomatic relief of bronchial asthma, emphysema and bronchiectasis. The Mudranes dilate the bronchi and liquefy mucus plugs. **DOSAGE:** Tablet; One tablet with a full glass of water 3 or 4 times daily as required. Divide tablet for child's dose. Elixir; Children, 1 cc for each 10 lbs. of body weight. May be repeated 3 or 4 times a day. Adult, one tablespoonful 4 times daily. All doses should be followed with a glass of water.

CONTRAINDICATIONS: Aminophylline/Theophylline is contraindicated in the presence of severe cardiac arrhythmias and patients with massive myocardial damage. Ephedrine, in presence of severe heart disease, extreme hypertension, and in hyperthyroidism. Phenobarbital, in porphyria and in patients with known phenobarbital sensitivity. Potassium Iodide, in pregnancy (to protect the fetus against possible iodine-induced depression of thyroid activity), in tuberculosis (produces gumma dissolution), and in acne; also in the presence of known iodide sensitivity. **PRECAUTIONS:** Aminophylline/Theophylline should be avoided in patients with massive myocardial damage and/or severe cardiac

arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdose. Potassium Iodide: Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing angular pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdose. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

HOW SUPPLIED: Mudrane and Mudrane GG available in bottles of 100 and 1000 tablets; Mudrane-2 and Mudrane GG-2 in 100s; Elixir in pints and half-gallons.

Federal law prohibits dispensing without prescription.



WILLIAM P. POYTHRESS & COMPANY, INC., RICHMOND, VIRGINIA 23261



Putting out the fires of arthritic pain

Rheumatoid arthritis can sometimes spread like wildfire, with joint after joint going up inflamed. "The usual onset is manifested by spotty joint involvement but an acute onset of symmetrical polyarthritis may be noted."^{*}

If aspirin fails, consider Butazolidin alka. Giving one capsule four times a day often provides prompt, pain-relieving, anti-inflammatory action to help restore joint mobility. The results you can get within a week can be maintained on as little as one or two capsules daily.

Serious side effects can occur. Select patients carefully (particularly the elderly) and follow them closely in line with the drug's precautions, warnings, contraindications and adverse reactions. For full details, please read the prescribing information. It's summarized on the back of this page.

Butazolidin[®] alka

Each capsule contains:

100 mg. phenylbutazone USP

100 mg. dried aluminum hydroxide USP

150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.

**Fire fighter
for arthritic
flare-ups.**

Butazolidin® alka

Each capsule contains:
100 mg. phenylbutazone USP
100 mg. dried aluminum hydroxide gel USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.
Ragan, C. The Clinical Picture of Rheumatoid Arthritis, in Arthritis, ed. 8, edited by J. L. Hollander and D. J. McCarty Jr., Philadelphia: Lea & Febiger 1972, chap. 21, p. 335.

Geigy

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of fever, sore throat, oral lesions (symptoms of blood dyscrasia), dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications: Children 14 years or less, senile patients, history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy, blood dyscrasias, renal, hepatic or cardiac dysfunction, hypertension, thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug, its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

(B)98-146-070-J (10/71)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardley, New York 10502

BU 10259

President's Pages



In the Temple Precincts — 1975 A.D.

The Scribes and the Pharisees brought a woman who had been caught in adultery, and placing her in the midst they said to Him, "Teacher, this woman has been caught in the act of adultery. Now in the law Moses commanded us to stone such. What do you say about her?" This they said to test Him, that they might have some charge to bring against Him. Jesus bent down and wrote with His finger on the ground. And as they continued to ask Him, He stood up and said to them, "Let him who is without sin among you be the first to throw a stone at her." And once more He bent down and wrote with His finger on the ground. But when they heard it, they went away, one by one, beginning with the eldest, and Jesus was left alone with the woman standing before Him. Jesus looked up and said to her, "Woman, where are they? Has no one condemned you?" She said, "No one, Lord." And Jesus said, "Neither do I condemn you; go, and do not sin again." —John 8: 3-11.

Last month an incident occurred which should be a concern of every physician in this state. As your President and representative, it caused me a considerable amount of soul searching and concern about the proper action. Briefly the facts are these: A 23-year-old woman had been receiving prenatal care from a physician for her third child. She first promised to pay his fee, but later found she was unable to do so. The doctor instructed her about how to qualify for Medicaid, but she never made application. In November 1974, after having failed to pay the doctor for her care or to apply for Medicaid the doctor notified her that he was terminating his services as her physician and made arrangements for her to be cared for at the County Health Department. The woman failed to go for prenatal care at the Health Department and went into labor on Saturday, February 15, 1975. Her former physician was contacted, but he refused to take up the case again. It was alleged that 20 other physicians in the area were contacted, and they refused to deliver her. (Although where they might be practicing, outside of Florence, is something of a mystery.) She tried to enter the Marion County Hospital and was refused admission because there was no physician to admit her. She finally was delivered by an attendant in the ambulance outside the Marion County Hospital. Fortunately, both mother and infant survived in good condition. During the following weeks I have received many calls and letters. Some demanded that the doctor be investigated and prosecuted. Others defended his actions. I have taken two actions. One negative and one positive. In the negative sense I have not ordered any investigation of this physician. From all information that I have been able to gather, he acted entirely within the ethical

standards of the medical profession. Three months before the delivery he informed the woman he would not deliver her and made arrangements with the County Health Department to continue her prenatal care. The woman apparently did not avail herself of this opportunity. Also there has been no formal complaint made to the South Carolina Medical Association either by the woman or on her behalf by someone else. This I feel is a necessary step before an investigation of any physician is undertaken.

At this point, many physicians may say, "I realize this man acted within ethical limits, but what of the moral obligation to render emergency care?" And regardless of what anyone may say, a delivery is a potential emergency at the very least. Ninety-five per cent of women may deliver without any complications at all; but in that other 5 per cent of cases a physician is needed and needed desperately. Many physicians (including myself) would have responded to this woman's needs. But before we criticize this physician, let us look at the circumstances. This doctor is the only physician in a town of less than 2,000. He is only one person, and he can do just so much. It is easier to be available when you are a member of a partnership practicing in an urban community with a hospital fully staffed by residents and interns on a round-the-clock basis. When you are in your midfifties practicing by yourself in a small community with no night or weekend relief, the situation is a little different. As this physician himself remarked "I could do 500 deliveries in a month if I wanted to." A man in a rural community by himself has to draw the limit somewhere, before his coronaries draw it for him. The rural physician is discouraged in many other ways. It is difficult to be called at the last minute to deliver a woman with little or no knowledge of possible complications such as diabetes, hypertension, pre-eclampsia, Rh incompatibility, *etc.* If something goes wrong in this last minute situation, there is a high incidence of professional liability. Frequently it winds up with Dr. Knowitall, Professor of Obstetrics at Metrocolossal Medical University testifying against our rural physician with devastating results. If the rural physician seems a little more fee conscious than his urban colleague, it may well be because HEW has a much lower fee schedule for rural areas than it does for urban areas in South Carolina.

Regardless of your opinion about the physicians's actions, one thing is certain, and this is the positive action. Some formal system for emergency medical coverage is needed in every area of the state. At the present time your medical association plans to discuss methods of providing emergency services with county medical societies and hospitals in all areas of this state. The Rural Health Delivery System eventually may solve some of this problem.

But even with the finest of emergency medical care services there are two other factors that need to be conquered and probably never will. When I graduated from medical school over 25 years ago, Tinsley Harrison told our graduating class, "You may think that disease is your greatest enemy. But you are wrong. Your two biggest enemies are poverty and ignorance!" Those words are just as true today as they were then. We see examples in our practice every day.

The 300 pound diabetic who literally eats herself into the grave with a knife and fork.

The four pack a day smoker who believes that he will not eventually die a quick agonizing death from lung cancer or a slow suffocating death from emphysema.

The alcoholic with a liver below his umbilicus who is going to give up drinking—*some day.*

People who still drive 75 miles per hour without using seat belts.

And in this case we had a woman who "forgot" to go to the Health Department and was driven around the lower end of this state for 7 hours instead of going 18 miles down I-95 to the McLeod Infirmary in Florence where she would have been delivered with minimal difficulty.

Our friends of the Fourth Estate have a quick answer, "Crucify this doctor! Reprimand him! Take away his license!" Winston Churchill once said many years ago "To every complex problem, there is always a simple answer—neat, plausible, and completely wrong!" Assuming you wanted this quick easy answer and had the authority to enforce it, what would be accomplished? The first accomplishment, in the continuing absence of an accusation of a complaint which has not been proven, would be a violation of the doctor's rights under the 5th and 14th Amendments to the Constitution of the U.S. (not to mention the Constitution and Bylaws of the S.C.M.A). Our free press and many of the public often forget that all citizens of the U.S. enjoy these rights—not just their favorites of the moment. The second accomplishment would be that one more small town in South Carolina would be without a doctor. A third accomplishment would be a threat that would accelerate the decline of the dwindling number of physicians who still practice obstetrics in a rural community.

What do we really want? Doctors and all other citizens can agree, I believe, that we all want to provide the best possible medical care to all people in South Carolina. This is a complex problem with no easy answers. Through Emergency Medical Care plans and the Rural Health Delivery System and other methods, the S.C.M.A. is attempting to provide part of the answer. But if a woman whose lack of knowledge and ability keeps her from getting medical attention, it is a responsibility that all of us must share. It must be borne particularly by those legislators and all other citizens who have fought consistently all efforts to give the children of South Carolina a decent education under the guise of saving money. "Let him who is without sin among you be the first to throw a stone——"

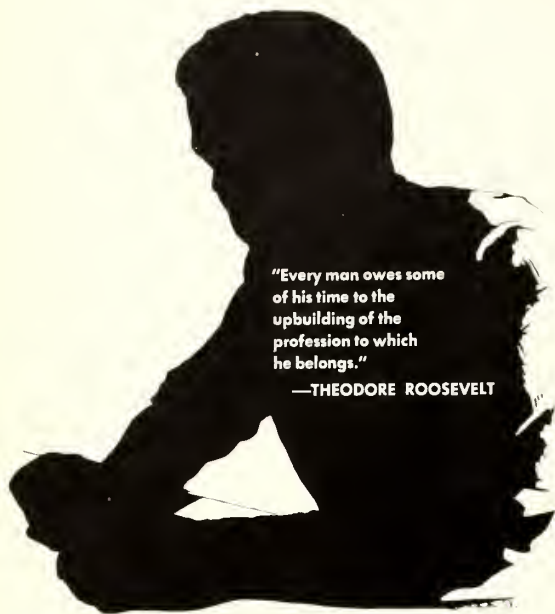
Donald G. Kilgore, Jr., M.D., President
South Carolina Medical Association



50 YEARS AGO

March 1925

Aiken County reorganized its medical society. There was much editorial discussion of annual physical examinations. The program for the annual meeting included a symposium on hookworm.



Attend the Annual Meeting of the South Carolina Medical Association!

May 4-7, 1975

ATLANTIC LANDMARK MOTOR INN
MYRTLE BEACH, S. C.

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone, or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

454 R

When diarrhea has his number...



Lomotil puts him back in the game.

Physicians and patients both want prompt control of the symptoms of diarrhea. A rapid, uncontrolled loss of fluids and electrolytes can cause a medical crisis, particularly in children, and in patients who are seriously ill, or in people who are badly undernourished.

Lomotil usually stops diarrhea promptly. This rapid action halts the emergency aspect of diarrhea

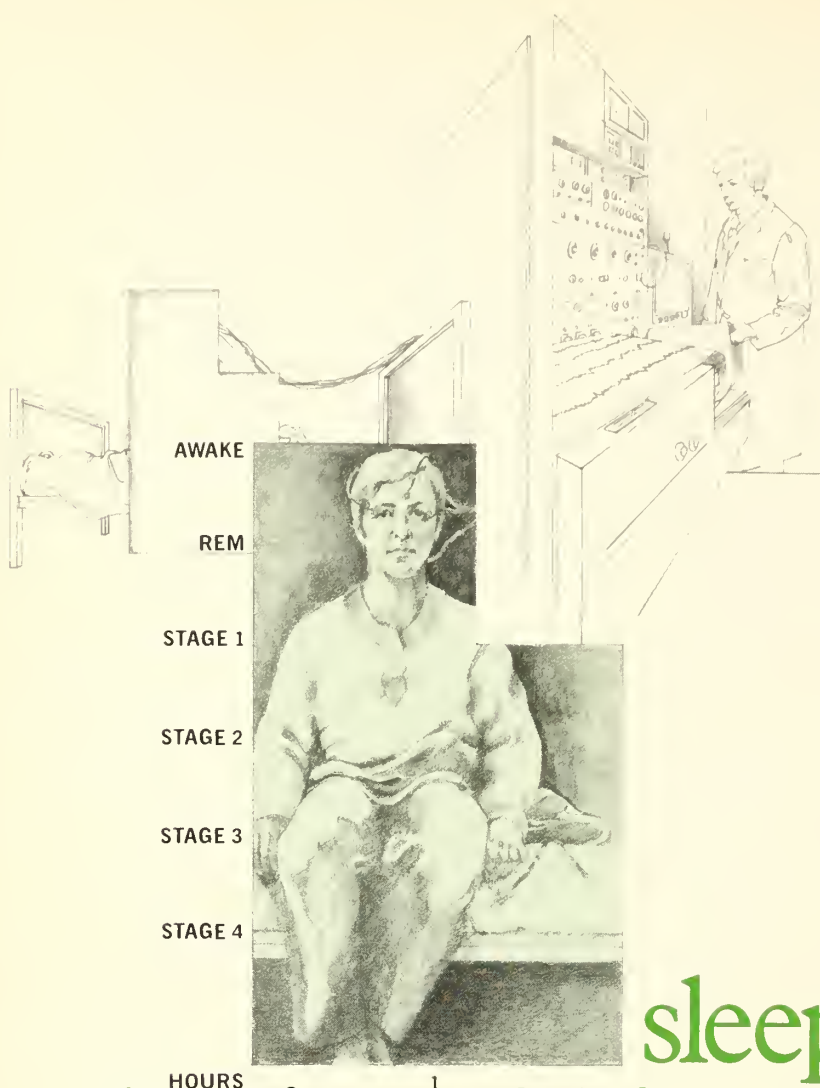
and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate antibiotic therapy should be given along with Lomotil.

Lomotil has few side effects, and those that do occur are generally mild.

Lomotil[®]
TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride 2.5 mg.
(Warning: May be habit forming)
atropine sulfate 0.025 mg.

Usually stops diarrhea promptly.



sleep
begins within
17 minutes, on average ...
an initial benefit of

Dalmane[®]
(flurazepam HCl) proved by a
**22-night clinical study of insomnia patients
in the sleep research laboratory and at home¹**

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.¹

Average Time Required
to Fall Asleep (4 Studies,
16 Subjects^{2,5})



confirmed by clinical studies in four geographically separated sleep research laboratories^{2,5}

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage²⁻⁵

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

REFERENCES: 1. Kales A, et al: *Arch Gen Psychiatry* 23:226-232, Sep 1970

2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971

3. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

when restful sleep
is indicated

Dalmane[®]

(flurazepam HCl)

One 30-mg capsule h.s. — usual adult dosage
(15 mg may suffice in some patients).

One 15-mg capsule h.s. — initial dosage for
elderly or debilitated patients.

- induces sleep within 17 minutes, on average
- reduces nighttime awakenings
- sustains sleep 7 to 8 hours, on average, without repeating dosage

ROCHE

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities.

Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

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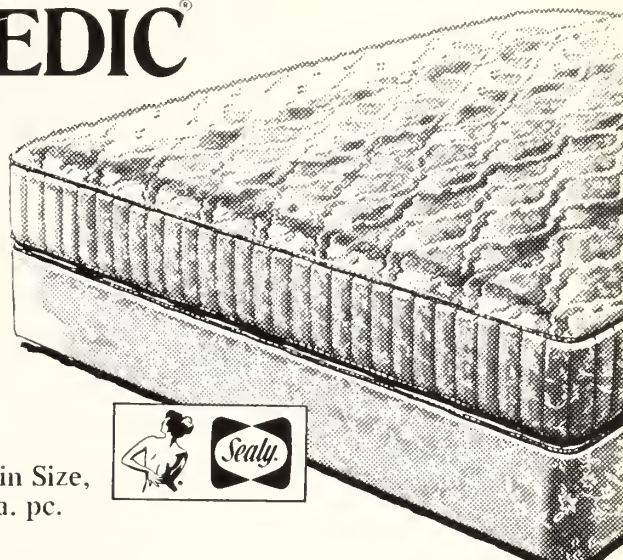
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Editorials

Better Than A Second Medical School!!!

Do you want to know a way to increase the supply of doctors in South Carolina that is better than establishing a second medical school? My way is quick, cheap (almost no expense involved), simple, direct, will supply both experienced and new doctors, specialists and family practitioners, majority groups and minority groups. If our state would just follow my simple directions immediately, in five year's time, South Carolina would have one of the highest doctor per thousand population ratios in the U.S. instead of one of the lowest. I guarantee it!

My way is so simple, so just, so equitable, so greatly needed that it probably will *never* happen.

All that is necessary for S. C. to attract immediately an abundance of medical talent is for the State Legislators to enact *now*, righteous medical liability laws! We all know the abominable and appalling condition of medical liability insurance nationwide. If South Carolina suddenly became a paragon of medical justice, there would be a rush to South Carolina by all those physicians all over the U.S. who are considering giving up private practice because of the problems and expense of getting liability coverage.

The Legislature could solve our problem now, if only they would. But, as H. L. Mencken said, "For every difficult problem there is a solution; simple, easy, quick, and wrong." Who knows?

EEK

The Nursing Shortage

Much has been said about the shortage of nurses in the hospitals of South Carolina. I have recently put my finger on one of the causes for this shortage in the hospitals of Columbia, and I imagine it applies elsewhere.

There is too much competition from government—county, state, and federal—for nurses. And I see this competition as unfair and deplorable. When government—V.A., Army, State Hospital, County Health Department — is able to offer greater (often far greater, even unreasonable) salaries, far more holidays, far easier work loads, no weekends, etc., etc., who can blame the nurses for succumbing to the allure of the easy life, even if it means bedding down with bureaucracy and ennui.

EEK

Image—MUSC

Your editor last weekend attended a weekend-long MUSC College of Medicine Faculty Conference on the image of MUSC. It was an exhilarating, jam-packed experience. Having never as much as set foot in the halls of MUSC, I felt a little like a pledge who had slipped into the highest fraternity councils, or like a novice who had stumbled into the sanctum sanctorum. Brains and knowledge were dripping everywhere. So were dedication and devotion. I would like to report to you some of my impressions of MUSC,

which, because I am an outsider, will necessarily be the image, and not the reality.

It is difficult to organize and cull the abundance of images, but here are some. *Growth of MUSC and Its Portent to the State*

Few doctors, even closely tied alumni, realize the tremendous growth that has taken place in just the last few years. For example, one of the major departments only five years ago had 4 interns (straight) and 14 or 15 residents for a total housestaff of 18 or 19, and 22 on the full time faculty. Today there are 27 interns and 55 residents for a total of over 80 housestaff and 60 full time faculty. Starting about now, this tremendous housestaff will be finishing up and drifting out over the state looking for patients. We have not yet but are just about to feel the impact throughout the state of the growth in products of MUSC.

Faculty of MUSC

There has been an enormous upgrading in both quantity and quality of faculty in the last few years. This great effort has taken much energy and has diverted the attention of the faculty from their obligations to the State of South Carolina. However, the faculty is now aware of this and is trying to deal with and satisfy this obligation without compromising what they see as their commitment to excellence. For instance, there is anxiety over the proper policy on out-of-state admissions. There are those who believe it is best to take more top grade out-of-state students to improve the student body and hope they will settle in this state. There are those who feel a responsibility to take an inferior applicant if he is a state resident. There is an uneasiness toward the place of research at MUSC. There is an (valid) apprehension that the people of South Carolina are not as committed to research, as aware of its values, and as dedicated to

its support as the faculty would hope. There is the question of how much research a teacher should do and vice versa.

Medical Students

The faculty was naturally very concerned about the student body. While every year it is more and more difficult to get in MUSC, the overall caliber of the student body is quite low in comparison to the national average, at least their background is deficient. Scholastic Aptitude Test scores are hundreds of points lower than those of students in most other medical schools and medical college aptitude test scores are appreciably lower. (This is due to insufficient preparation in South Carolina secondary schools and colleges and should be a worry for all of us interested in the welfare of South Carolina.) There is regret that the student fail rate is virtually zero. This inadequately motivates the poorer students and inadequately rewards the better students.

State Support

The MUSC faculty is aware of the tremendous financial support offered the institution by the people of South Carolina—for next year a budget of 77 million dollars with 42 million dollars in direct state support is hoped for. The faculty is aware that this increasing state support is in marked contradistinction to the sagging economic base of most private institutions—some of the greatest names in medical education.

My image of MUSC can best be summed up in the words of Dr. Thomas Gaffney in his summation, "The MUSC is not the greatest medical school in the U.S. It is not even one of the greatest. But it is *the most* exciting medical school in the entire country—exciting in its present efforts and in its potential."

These are some of my many impressions of IMAGE—MUSC.

EEK

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Each 30 cc contains:

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Atropine sulfate	0.0194 mg
Hyoscine hydrobromide	0.0065 mg
Powdered opium, USP	24.0 mg

(equivalent to paregoric 6 ml.)
(warning: may be habit forming)

Sodium benzoate (preservative) 60.0 mg

Alcohol, 5%

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Fall and winter coughs are back. Time to help clear the lower respiratory tract with the five Robitussins and Cough Calmers. All contain glyceryl guaiacolate, the efficient expectorant that works systemically to help increase the output of lower respiratory tract fluid. The enhanced flow of less viscid secretions soothes the tracheo-bronchial mucosa, promotes ciliary action, and makes thick, inspissated mucus less viscid and easier to raise. Available on your prescription or recommendation.

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Non-narcotic for 6-8 hr. cough control

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Each 5 cc. contains:
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Robitussin-DM in solid form for "coughs on the go"

COUGH CALMERS[®]

Each Cough Calmer contains:
Glyceryl guaiacolate 50 mg.
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Clears nasal and sinus passages as it relieves coughs

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Comprehensive decongestant action helps control cough and clear stuffy nose and sinuses. Non-narcotic.

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Glyceryl guaiacolate 50 mg.
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ROBITUSSIN-DM [®]	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
ROBITUSSIN-PE [®]	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
ROBITUSSIN [®] -CF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
COUGH CALMERS [®]	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

THE STORY OF PEDRO

Pedro was a very small, but very honest business man. He was born and raised and hoped to die in San Carlos. Outside of being very old, his hometown was not famous and probably very few outsiders knew of its existence. However, Pedro and his little family were very happy. Pedro was a peanut vendor as his father was before him. He was a good peanut vendor and was proud of his profession and his heritage.

In his younger days, he had taken special training in the arts of vendoring peanuts and after years of struggle and privation, had built up a good business. His cart was sound, his peanut roaster was small but of excellent quality and lately he had finally saved enough to buy the large, brightly colored umbrella which everyone agreed, added a dash of elegance to his establishment.

Then one day, by decree of the provincial governor, an institution was established in Pedro's home town to be known as The Peanut College of San Carlos. This was a beautiful, red brick, glittering building, ten stories high in the air. A large faculty was imported from distant lands. Bulletins were placed in the town square telling of the numerous wonders of this great building. According to these bulletins, this great college roasted their peanuts in a shiny oven with red and green blinking lights and instead of an umbrella, there was a large electric sign which cost many pesos.

Pedro's friend, who was also an old customer, was sad now when he visited

Pedro. He was the tax collector for the district and found that he needed many more pesos from the people so that the Peanut Center could operate at peak efficiency and turn out peanuts which were only of the very highest grade. As with many other old customers of Pedro's, the tax collector now bought his peanuts from the Peanut College of San Carlos since, had not the provincial governor said that the red and green lights must make better peanuts? Pedro's business declined and in order to meet the demands of the tax collector, it was necessary to sell, one at a time, his umbrella, then his cart and finally his roaster. The next possession to go would be his home but Pedro, being a former honest small businessman realized this, sold his home and moved his now unhappy little family, to another district where there was no Peanut College. Here, he began anew and is now, again, a well established, honest small business man with a cart, roaster and brightly colored umbrella. Pedro now realizes that the Peanut College is a basically good investment of provincial pesos but, why, he wonders, did it have to be built in San Carlos where he and the other small, honest peanut vendors were made to feed the mouth that bites them.

This article appeared in *The Scribe*, formerly published by Charleston County Medical Society, in April 1959. The anonymous author believes it is time to revive Pedro. Your editor thinks this issue, concentrating on IMAGE—MUSC, would be an appropriate time to exhume Pedro.

EEK

Letter to the Editor

S. C. Medical Care Foundation
P. O. Box 11188
Columbia, S. C. 29211
Attn: Kenneth N. Owens, Pres.

Dear Sirs ;

Recently I received the second of two recent mailings from you with your date of December 29, 1974 in which you asked me as "one of the original members" to sign the enclosed membership card and return it by mail.

The first solicitation that I recall receiving which indicates the true purpose of the foundation, was not dated but came to me about two months ago. I read it and was greatly disturbed by it. I discussed its contents with several contemporary trusted colleagues and I found that they were as disturbed as I. I did not sign the enclosed card but kept it, awaiting further information or possibly inspiration.

I did not remember joining the foundation but I have been informed by your secretary that I signed a card to join about eighteen months ago. At that time I did not realize that you planned to help the government set up HMO's and PSRO's. On the contrary I had thought the organization's purpose was to help thwart the march of socialized medicine. I would like to have my name removed from your roll and relinquish my "original" membership status.

I find that I do not have words or information to refute the "facts" that were stated by you in your recent solicitation but I have a feeling that members of the

medical profession are being herded out of fear into visible groups called Medical Care Foundations so that these foundations can be given instructions directly from the political establishment and so that compliance with socialized medical edicts can be enforced by putting pressure on these so called "voluntary" organizations.

I am delighted to hear that only 600 medical practitioners in South Carolina came into the fold upon your first solicitation. Since the State Board of Medical Examiners listed 2,800 physicians and eight osteopaths last year, you got less than 25%. This indicates to me that many others had reservations similar to those which I now feel and therefore that there must be an overwhelming majority of doctors in the state who do not agree with this governmental regimentation.

A copy of this letter is being sent to the editor of the JSCMA, with the request that it be printed and commented upon if the editor so desires. Maybe he will wish to take a "straw ballot" to learn first if other doctors became "original members" by mistake, and second if others who may have signed the card and sent it in would like to resign.

J. R. Paul, Jr., M.D.

Note: Over 1,400 physicians are now members of the S. C. Medical Care Foundation and are endorsing its activity to implement PSRO.



FINANCIAL CORNER



Dow Theory Forecasts has furnished JSCMA with a complimentary subscription to its weekly forecast. The editor will select one stock a month from those recommended, will "buy" a round lot, and we will keep a running tabulation.

STOCK OF THE MONTH

RCA—Reflecting a 69% drop in fourth quarter net income (\$16.6 million vs. \$53.4 million), RCA reported sharply lower 1974 earnings. For the year, per share figures fell 38% to \$1.45 from \$2.39 the year before. The sharp drop in profits resulted from severe weakness in the company's consumer products area. Television sales were weak and competition was intense, making it impossible to pass on rising material and operating costs.

RCA's food processing and household furnishings operations were also caught in a cost-price squeeze. While weakness will undoubtedly carry over into the first half of 1975, improvement should start to appear by the middle of the year. We feel these quality shares are underpriced at current depressed levels and deserve consideration for a combination of income and recovery potential.

Price: \$11 Div.: \$1.00 Yield: 9.1

JSCMA Portfolio of Dow Recommended Stocks

Stock	Date	Purchase Price	Present Value	Dividends (added yearly)
RCA	1 Feb 75	100x\$11=\$1100	\$1100	\$1.00/share

If you like this and want other advice from Dow, let me know.

PSRO — Status Report

The South Carolina Medical Care Foundation has submitted a final proposal to the Department of Health, Education, and Welfare for designation as the Professional Standards Review Organization in South Carolina.

The Medical Care Foundation represents over 55% of the physicians in South Carolina, with a current membership of over 1,400. The general attitude of these physicians has been an acceptance of the challenge put before them. They recognize that PSRO is law and since this law must be implemented, it should be done under the control of the practicing physicians, rather than an organization that does not represent their interests.

Representatives of PSRO have travelled extensively throughout the state in recent weeks conducting meetings with various medical staffs and organizations to explain the Medical Care Foundation's plan for PSRO. A major area of concern has been the development of criteria, standards, and norms to be used in the PSRO program. A committee of twenty-five physicians representing the major specialty societies has been actively engaged in developing this criteria. When this task is completed the criteria, standards, and norms will be distributed to every hospital in South Carolina for their review and comment. Modifications may be made by local medical staffs and approved by the Foundation Committee for use in the PSRO program. This committee will be responsible for maintaining the quality of care throughout the state.

An important question PSRO representatives have been confronted with concerns the monitoring procedure of the PSRO. The PSRO will monitor the activity in each hospital through data collected on an abstract form. Deviations from the established norms of care will be referred to the local medical staff for their review. The local medical staff will determine what action, if any, is necessary. Site visits by the PSRO central office staff will be conducted upon the request of the local medical staff. These site visits will

take the form of technical assistance to aid in the implementation of the PSRO program in the individual hospitals.

The Blue Cross/Blue Shield organization and Department of Social Services will continue their monitoring procedures to evaluate PSRO performance, although the scope of this monitoring is not yet clear. The responsibility for final determination of payment on the medical necessity of hospital stays rests with the PSRO once the program is in operation in a hospital.

It is anticipated that PSRO will begin implementing the PSRO program in hospitals no later than September of this year.

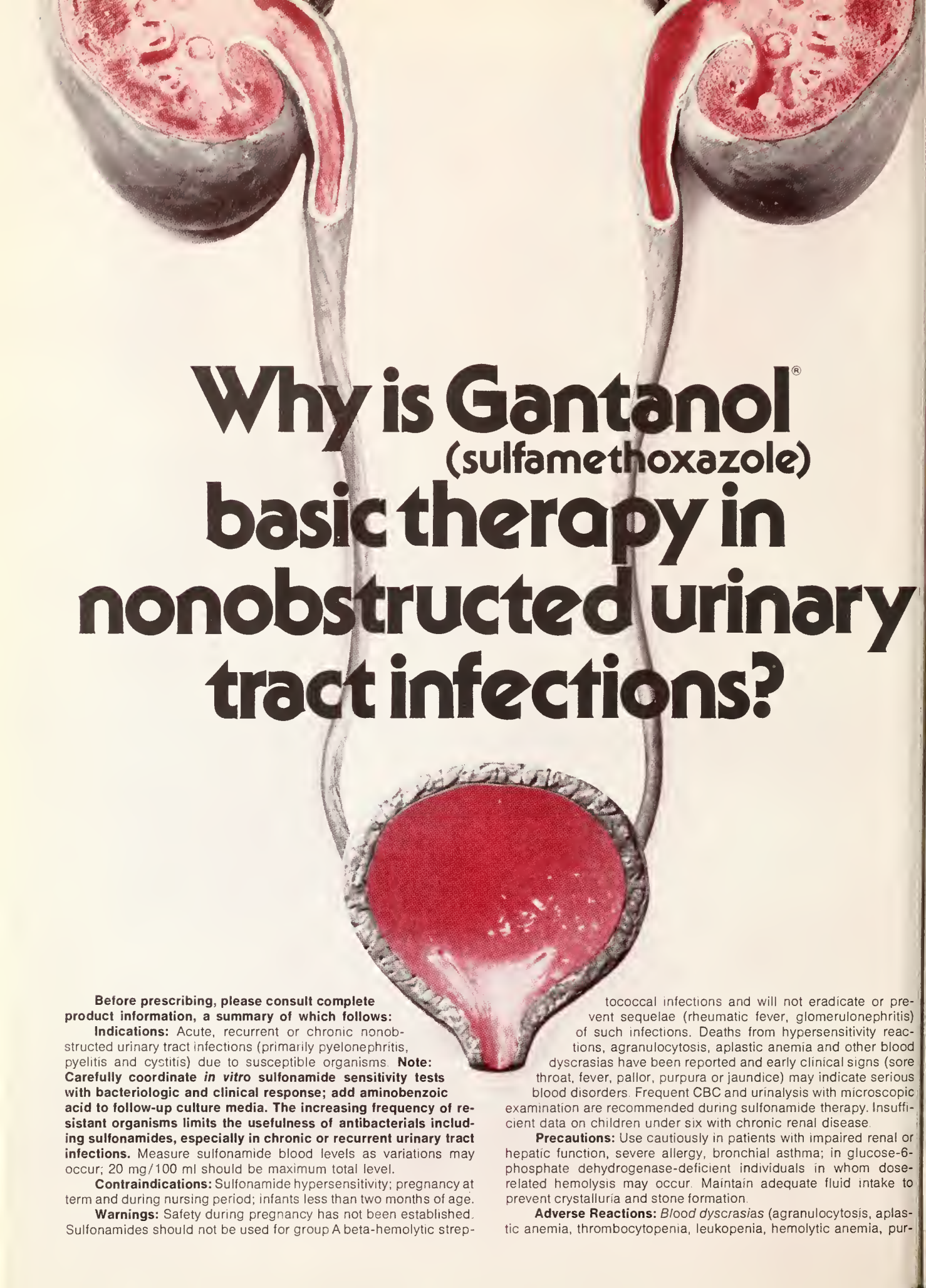
BOOK REVIEW

THE UNCERTAIN MIRACLE by Vance H. Trimble. Doubleday & Co., Inc. Garden City, N. Y., 1974. Pp. 236. \$6.95.

This book is a very well documented, well written text for the professional and non professional mind to understand hyperbaric oxygen. It shows the author has done his homework very thoroughly. The author at times seems frustrated in that hyperbaric oxygen is not universally used. At times he ponders why modern medicine has not accepted hyperbaric oxygen and why everyone cannot see the exciting value of hyperbaric oxygen.

The historical detail and progression to present is well presented by Mr. Trimble. It is enjoyable reading for the lay and medical minds. One wonders when reading certain portions of this book why modern medicine has not accepted this form of treatment thoroughly. However, in the last chapters, Mr. Trimble does explain some of the complications, the problems, and the costs. For anyone studying the use of hyperbaric oxygenation, this book is a must for reading. It is well documented. It has good depth of investigation. It presents the picture of hyperbaric oxygenation, fairly. I do think Mr. Trimble has found that medical men do progress slowly into new fields. Perhaps too slowly, but when they go, they go thoroughly and surely.

Foster Marshall, M.D.



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Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic strep-

tococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, pur-

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pura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasps.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasps.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.



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(methacycline HCl)

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**

Usage in pregnancy. (See above **WARNINGS** about use during tooth development.) Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate observed in premature infants given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: **Gastrointestinal** (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN—apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea: In uncomplicated gonorrhea, when penicillin is contraindicated, Rondomycin[®] (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule: 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of Rondomycin[®] (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia: 900 mg daily for six days.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

SUPPLIED: Rondomycin[®] (methacycline HCl): 150 mg and 300 mg capsules; syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev. 6/73



WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512



**When the focus is on bronchitis due to
susceptible strains of *H. influenzae* and pneumococci***

Rondomycin[®] 300 mg.
[methacycline HCl] Capsules

Delivers from the very first dose:

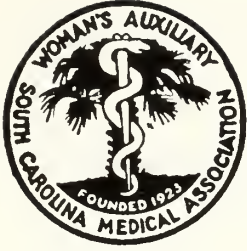
**Studies show that after the first dose serum levels rapidly rise above
minimum *in vitro* inhibitory concentrations**

*Since many strains are known to be resistant, routine sensitivity testing is recommended

**MEDICAL UNIVERSITY OF SOUTH CAROLINA
SESQUICENTENNIAL DEPARTMENTAL SEMINARS
OF THE COLLEGE OF MEDICINE**

- | | |
|-------------|--|
| April 4-5 | Surgery — John H. Davis, M.D. of the University of Vermont, Visiting Speaker. |
| April 10-12 | Ophthalmology (Ninth Annual Residents Conference) — Paul Henkind, M.D., Ph.D. of the Montefiore Hospital and Medical Center, Bronx, N. Y., Herbert E. Kaufman, M.D. of the University of Florida, and Dan B. Jones, M.D. of Baylor College of Medicine, Houston, Visiting Speakers. |
| April 17-18 | Pathology — Thomas M. Peery, M.D. of George Washington University, Visiting Speaker. |
| April 24-26 | Obstetrics and Gynecology — Allan C. Barnes, M.D. of the Rockefeller Foundation, New York, and Arthur L. Herbst, M.D., of Harvard Medical School, Visiting Speakers. This seminar is held in conjunction with the Tenth Annual Meeting of the Thegos Society. |
| May 2-3 | Pediatrics—Robert W. Winters, M.D., of Columbia University, and Albert B. Sabin, M.D., of the Medical University of South Carolina, Visiting Speakers. This seminar will be held in conjunction with the meeting of the South Carolina Pediatric Society and the South Carolina Chapter of the American Academy of Pediatrics. |
| May 16-17 | Thoracic Surgery — Denton A. Cooley, M.D., Surgeon-in-Chief of the Texas Heart Institute, Houston; W. Leigh Thompson, Jr., M.D., Ph.D., of Case Western Reserve University; Priv. Dr. K. Messmer of Universitäts-Klinik, Munich, Germany; Karl E. Arfors, M.D., of Pharmacia, Upsala, Sweden; and George A. Clowes, Jr., M.D., of Harvard University, Visiting Speakers. |

Please notify the appropriate department if you expect to attend. Medical University of South Carolina, 80 Barre St., Charleston, S. C. 29401.



WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION

A Tribute To You On Doctor's Day

Doctor's Day was originated in Barrow County, Georgia, in 1933 and was introduced to the Southern Medical Association in 1934 and adopted in 1935. The purpose being to honor members of the medical profession—living and dead.

The date of March 30 was not chosen at random but to commemorate one of the greatest discoveries in medical history. It was on this date in 1842 that Dr. Crawford W. Long, the famous Georgia physician, first used ether as an anesthetic agent in a surgical operation thereby providing mankind with the blessedness of freedom from pain and suffering during surgery.

Doctors' wives are interested in the welfare of medicine because of the unique manner in which they become eligible. There's only one way to get into our organization. Each one of us was handpicked by a doctor. Each of us thinks that doctor is great and we want the community to think so too.

If the wife takes her auxiliary membership seriously, she not only brings credit to medicine through her service projects, but because of being informed, she says the right thing in her many conversations with the public. This is one reason that it is important for our two organizations to work closely together. We appreciate knowing how to answer the clerk, the butcher and the baker, who are getting plenty of misinformation about doctors from labor publications. Through know-

ing how to answer questions in our person-to-person contacts, we bring credit to you.

We cringe when the press maligns you, for we know how great you are, even without the Harris poll, which again has placed you first in the nation, most trusted by the public. We're mighty proud to be married to you.

We feel pretty much like little Janie White, who was so proud that her daddy was the town doctor that anytime she was asked her name, she answered that she was "Doctor White's daughter." When her mother noticed her unseemly pride, she told Janie that when someone asked her name not to say, "I'm Doctor White's daughter," but to simply say, "I'm Janie White." A few days later, Janie had a substitute teacher. Getting acquainted with the children, the teacher circulated, speaking to each. When she came to Janie, she said, "Now, let's see. Aren't you Doctor White's daughter?" Sadly Janie shook her head, saying, "I thought so, but Mother says no."

We do bask in your glory, but we try to be modest.

Like little Janie, we sometimes need specific directions, but if you give us that, we'll not only break our necks for you, but we'll even know how to be a credit to you.

Most Sincerely,
Billie Brady
President, SCMA Auxiliary

Woman's Auxiliary to South Carolina Medical Association

52nd Annual Convention

Landmark Motor Inn
1501 South Ocean Boulevard
Myrtle Beach, South Carolina

PROGRAM

Registration

Coffee Shop Area, Landmark Motor Inn

May 4, 5, 6, 7, 1975

Sunday, May 4 -----3:00- 5:00 P.M.

Monday, May 5 -----8:30-11:30 A.M.

Tuesday, May 6 -----8:30- 9:30 A.M.

Sunday, May 4, 1975

4:00 P.M. Finance Committee Meeting, President's Suite #526, Landmark

Monday, May 5, 1975

8:30-9:30 A.M. Complimentary Continental Breakfast, Coquina Room, 4th Floor, Landmark

10:00 A.M. Executive Board Meeting, Coquina Room, 4th Floor, Landmark
Mrs. Wayne C. Brady, President, presiding.

1:30 P.M. Luncheon with Husbands, Grand Strand Ball Room, 4th Floor, Landmark
Guest Speaker: Governor James B. Edwards

3:00 P.M. Round Table Conference, Coquina Room, 4th Floor, Landmark

7:00 P.M. Auxiliary Social Hour Grand Strand Ball Room, 4th Floor, Landmark

8:00 P.M. Buffet Dinner and Entertainment by Miss South Carolina

Tuesday, May 6, 1975

8:30-9:30 A.M. Complimentary Breakfast, Coquina Room, 4th Floor, Landmark

10:00 A.M. House of Delegates Meeting, Colonial Room, Pine Lakes International Country Club
Mrs. Wayne C. Brady, President, presiding.

1:00 P.M. Membership Luncheon, Pine Lakes International Country Club
Guest Speaker: Mrs. Norman Gardner, 1st Vice President, AMA Auxiliary

2:30 P.M. Honored Guests: Past State Presidents of Auxiliary
Post-Convention Board Meeting, Colonial Room, Pine Lakes International Country Club

7:00 P.M. Mrs. Wayne C. Brady, presiding.
SCMA Reception and Banquet, Grand Strand Ball Room, 4th Floor, Landmark

Donald C. Kilgore, M.D., President, South Carolina Medical Association, presiding.

Guest Speaker: Neal Pearce, Author, Lecturer, & Political Commentator

Wednesday, May 7, 1975

State Auxiliary Breakfast, Grand Strand Room I, 4th Floor, Landmark
Auxiliary Workshop to follow in Coquina Room, 4th Floor, Landmark

PRE-REGISTRATION FORM
FOR CONVENTION
WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION
May 4-7, 1975

HEADQUARTERS: Landmark Motor Inn, 1501 South Ocean Boulevard,
Myrtle Beach, S. C. 29577 — Phone 803-448-4371

Please Print or Type

Name _____ First Name _____

Address _____

City _____ Zip _____

Where staying in Myrtle Beach _____

Check Desired Activity and Include Check, Payable to Woman's Auxiliary to SCMA

Sunday, May 4, 1975

Registration 8:30-11:30 A.M., Coffee Shop Area, Landmark Motor Inn

Monday, May 5, 1975

Registration 8:30-11:30 A.M., Coffee Shop Area

- () 8:30-9:30 A.M. Complimentary Continental Breakfast, Coquina Room, 4th Floor, Landmark
- 10:00 A.M. Executive Board Meeting, Coquina Room, 4th Floor, Landmark
- () 1:30 P.M. Luncheon with Husbands, Grand Ball Room, 4th Floor, Landmark
Special Guests: Gov. and Mrs. James Edwards
Price per person: \$5.25
- () 7:00 P.M. Auxiliary Social Hour, followed by Buffet Dinner, 8:00 P.M.
Grand Strand Ball Room, Landmark Motor Inn. Fabulous entertainment by Miss South Carolina, Cheryl von Lehe.
Husbands cordially invited. Price \$12.00 per person.

Tuesday, May 6, 1975

Registration 8:30-10:00 A.M., Coffee Shop Area, Landmark Motor Inn

- () 8:30-9:30 A.M. Complimentary Continental Breakfast, Coquina Room, 4th Floor
- 10:00 A.M. General Meeting, House of Delegates, Colonial Room, Pine Lakes International Country Club
- () 1:00 P.M. Membership Luncheon, Past State Presidents Honored. Pine Lakes International Country Club, Mrs. Norman Gardner, 1st Vice President, AMA Auxiliary, Speaker
Price \$6.00 per person
- 2:30 P.M. Post-Convention Board Meeting, Colonial Room, Pine Lakes Country Club
- () 7:00 P.M. SCMA RECEPTION AND BANQUET, Grand Ball Room, 4th Floor, Landmark. Remind your husbands to secure these tickets through SCMA

REGISTRATION FEE FOR EACH MEMBER — \$1.00

Reservation forms with check, should be mailed prior to April 25, 1975, Mrs. Laurie N. Ervin, 44 Stillwood Drive, Greenville, S. C. 29607. Tickets will be held at pre-registration desk in Coffee Shop Area of Landmark Motor Inn during registration hours ONLY.

NOTE: Pre-registration for the various activities, with your check, must be made by **April 25, 1975 DEADLINE**. No tickets available at convention.

This is necessary to help make YOUR CONVENTION a success. Thank you!



Bioequivalence

Form with fields for patient information, including name, address, and date.

NAME	_____
ADDRESS	_____
DATE	_____

the weight of scientific opinion:

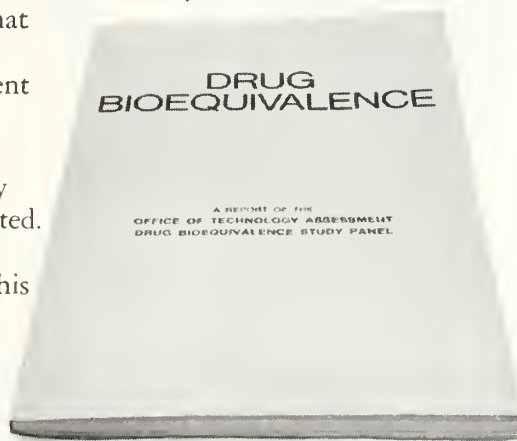
If the pharmacist substituted a chemically equivalent drug for the one you have specified for your patient—could you be certain of that product's safety and effectiveness simply because the chemical content was the same?

Definitely not, unless bioequivalence tests and other quality assurance checks had been conducted. The pharmaceutical industry and many scientists have maintained this position for years, but others have questioned it. Now the Office of Technology Assessment of the Congress of the United States has reported on the issue in its Drug Bioequivalence Study.*

Here are a few definitive statements in the O.T.A. report:

"...the problem of bioinequivalency in chemically equivalent products is a real one. Since the studies in which lack of bioequivalence was demonstrated involved marketed products that met current compendial standards, these documented instances constitute unequivocal evidence that neither the present standards for testing the finished product nor the specifications for materials, manufacturing process, and controls are adequate to ensure

that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.



"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and

(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or
(c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

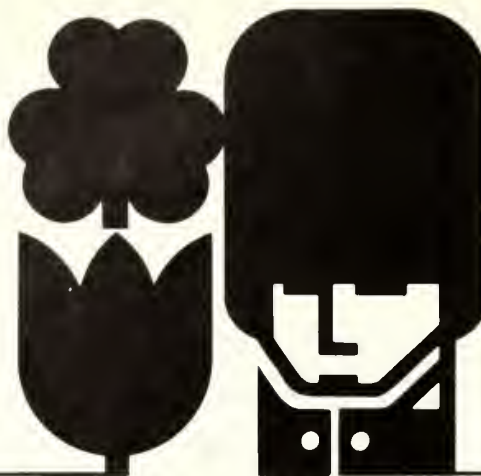
The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...



Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

protecting the integrity of your prescription



SOUTH CAROLINA MEDICAL ASSOCIATION



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Another Non-Regimented INTRAV Deluxe Adventure

Rocky Mountain Spotted Fever Advisory

—By the S. C. Department of Health and Environmental Control—

This is the time of year to increase the index of suspicion for Rocky Mountain Spotted Fever, also called tick typhus or American tick-borne spotted fever.

The South Carolina Department of Health and Environmental Control (DHEC) has observed a significant increase in the incidence of Rocky Mountain Spotted Fever in the state during the past 6 years. The first cases are usually reported in early May, with the peak number of cases coming in August.

Physicians are asked to be on the alert for febrile illnesses which follow tick bites or exposure in tick-infested areas. When Rocky Mountain Spotted Fever is suspected, serological confirmation is available from the Department of Health and Environmental Control Laboratory at 2600 Bull Street in Columbia. At least 2 serum specimens, collected 2 weeks apart, should be submitted to the State Laboratory in order to determine a rise in antibody titer. All cases should be reported to the DHEC Division of Epidemiology via the local county health department.

Severe headache, listlessness, myalgia, sudden chill, rapid rise in temperature and rash are characteristic symptoms of the disease and when a history of exposure to ticks is also present, the diagnosis is suggested. Symptoms may occur from two to twelve days after a person has been bitten by an infected tick. The distinctive rash usually appears on the extremities during the third day of the disease; early rash may resemble measles or other rash illnesses.

When diagnosed early, Rocky Mountain Spotted Fever can be treated successfully by the tetracycline drugs or chloramphenicol. Vaccines are available, but due to the questionable effectiveness of current vaccines and the low risk of contracting the disease, the vaccine is recommended only for special situations such as laboratory personnel working with *Rickettsia rick-*

settsii and persons whose occupations result in repeated exposure to ticks in endemic areas.

Only live ticks that are removed from human beings should be mailed to the following address to determine if the tick is infected with a rickettsial organism.

Division of Vector Control
South Carolina Department of Health
and Environmental Control
2600 Bull Street
Columbia, South Carolina 29201

Due to the large volume of ticks submitted, we cannot examine those removed from animals or the environment.

It is requested that all live ticks submitted be placed in a medicine vial containing a small strip of paper towel moistened with *one drop* of water. Attached information should include date, locality, host, collector and telephone number of physician or patient. The sender can expect a telephone reply if tests are positive.

If a positive tick was removed from a patient whose signs and symptoms are compatible with a diagnosis of Rocky Mountain Spotted Fever, treatment can be initiated.

Fifty-five cases of Rocky Mountain Spotted Fever were reported in South Carolina during 1974, including five fatal cases. The fatalities were two young girls, ages two and five; a 49-year-old woman, and a couple in their forties. More than three-fourths of the cases reported occurred in the Piedmont or above the fall line.

The American dog tick, *Dermacentor variabilis*, is the most prevalent tick in South Carolina and a potential carrier of tick-borne typhus. Not all ticks are infected. Even in heavily-infested areas, only about one tick in twenty is infective and, therefore, able to transmit Rocky Mountain Spotted Fever.

CONTINUING EDUCATION CRUISE SEMINAR

May 7 - 14, 1975

A 7-day scientific seminar cruise, to be held aboard the luxurious M/S Victoria, May 7-14, 1975, sailing from Charleston, South Carolina and calling on the ports of San Juan and St. Thomas, is being sponsored by the Division of Continuing Education of the Medical University of South Carolina, the North Carolina Medical Society, and the South Carolina Medical Association.

Outstanding faculty have been chosen for lectures and presentations on endocrine and metabolic topics, a variety of psychiatric topics, and cardiology. Twenty-two CE units will be awarded for AMA Recognition Award.

This cruise is arranged by Southern International Travel Corporation specializing in international group and convention services. The M/S Victoria has a capacity for only 430 passengers, so reservations will be taken on a first come-first served basis. A \$100.00 deposit will insure reservation. A full color brochure and description of the course can be obtained by writing:

MEDICAL SEMINAR CRUISE
Southern International Travel Corporation
Post Office Box 19372
Raleigh, NC 27609

Cabin rates range from \$360 to \$640. Your entire family and friends may join you on this cruise.

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Disruptive anxiety usually meets its match here.

- Often effective when reassurance and counseling are insufficient.
- Three dosage strengths to meet most therapeutic needs.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

Precautions:

ORAL: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six.

INJECTABLE: Keep patients under observation, preferably in bed, up to three hours after initial injection; forbid ambulatory patients to operate vehicle following injection; do not administer to patients in shock or comatose states; use reduced dosage (usually 25 to 50 mg) for the elderly or debilitated and for children age twelve or older.

ORAL AND INJECTABLE: Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating compounds such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual



precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduc-

tion; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

With the injectable form, isolated instances of hypotension, tachycardia and blurred vision have been reported; also hypotension associated with spinal anesthesia, and pain following I.M. injection.

Usual Daily Dosage: Individualize for maximum beneficial effects. **Oral: Adults:** Mild and moderate anxiety and tension, 5 or 10 mg t.i.d. or q.i.d.; severe states, 20 or 25 mg t.i.d. or q.i.d. **Geriatric patients:** 5 mg b.i.d. to q.i.d. (See Precautions.)

For Parenteral Administration: Should be individualized according to diagnosis and response. While 300 mg may be given during a 6-hour period, do not exceed this dose in any 24-hour period. To control acute conditions rapidly, the usual initial adult dose is 50 to 100 mg I.M. or I.V. Subsequent treatment, if necessary, may be given orally. (See Precautions.)

Supplied:

Oral: Librium® (chlordiazepoxide HCl) **Capsules**—5 mg, 10 mg, 25 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 50, available singly and in trays of 10.

Libritabs® (chlordiazepoxide) Tablets—5 mg, 10 mg and 25 mg—bottles of 100 and 500.

Injectable: Librium® (chlordiazepoxide HCl) **Ampuls**—Duplex package consisting of a 5-ml dry-filled ampul containing 100 mg chlordiazepoxide HCl in dry crystalline form, and a 2-ml ampul of Special Intramuscular Diluent (for I.M. administration). Before preparing solution for I.M. or I.V. administration, please consult package insert for instructions on preparation and administration of solutions. Boxes of 10.



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Nutley, New Jersey 07110

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Please see preceding page for summary of product information.

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THE JOURNAL

SOUTH CAROLINA MEDICAL ASSOCIATION

ACUTE MONTEGGIA LESIONS
ADMISSION TO MEDICAL SCHOOL
HYSTEROSCOPY

VOLUME 71

APRIL 1975

NUMBER 4

BECOTIN®
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Both often



Predominant
psychoneurotic
anxiety

Associated
depressive
symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor

neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

MAY 12 1975

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

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Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

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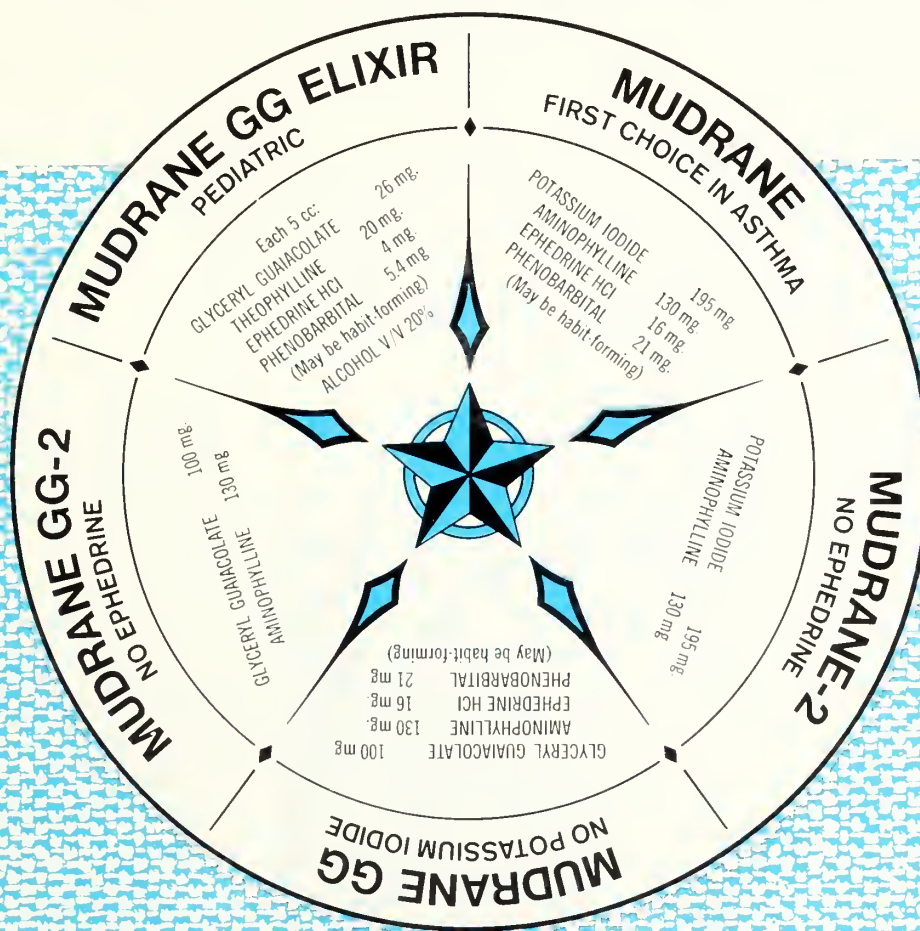
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ACUTE MONTEGGIA LESIONS IN CHILDREN*

JOHN L. EADY, M.D.**

In 1814, two cases of fracture of the proximal ulna associated with dislocation of the radial head were described by Giovanni Monteggia, and this type of injury has since come to bear his name. Until 1940, the bulk of the literature dealing with this injury was found in other languages. For example, in the twelve years prior to 1940, thirty-four articles were published, of which only two were in English.¹ Since then, a number of excellent articles have appeared in the English literature which, while drawing attention to this lesion, have produced conflicting opinions regarding its etiology and incidence in children.

Using investigation of clinical material, radiologic studies, schematic representations and review of the literature, the factors of etiology, incidence, diagnosis and treatment of the acute lesion in children shall be presented.

DESCRIPTION

As described by Monteggia, this injury was defined as a fracture of the ulna between the proximal and medial third and the base of the olecranon, plus the radial

head dislocation (Fig. 1-1). Now however, any fracture of the ulna with an associated head dislocation is usually called a "Monteggia." Bado² suggested that the entire gamut of injuries be described as "Monteggia lesions," and the recent literature has tended to follow this recommendation.

The lesion is divided into three basic types:

- a. Type I: Fracture of the ulna with anterior dislocation of the radial head.
- b. Type II: Fracture of the ulna with posterior dislocation of the radial head.
- c. Type III: Fracture of the ulna with lateral dislocation of the radial head.

There is also a "Type IV" lesion which is described as a fracture of both bones of the forearm in the proximal third with



*This paper was presented at the South Carolina Orthopedic Association meeting in September 1974 and won first prize in the annual competition open to all orthopedic residents in training in South Carolina. The author was awarded an appropriate prize.

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ACUTE MONTEGGIA LESIONS

anterior dislocation of the radial head. Both bones are felt to fracture at the same level by some authors, but we have seen this to be at different levels in a young adult.

INCIDENCE

The age of incidence has been reported from two months to fourteen years of age but occurs most frequently between seven and ten years.

Overall incidence varies from one per thousand fractures¹ to 1.7 per cent.³ Comprehensive figures are not available, but it is probable that the true incidence varies with population, geography and awareness of the physician.

The incidence of each type of injury is represented in Figure 1-2, which includes both children and adults. Type I lesions are in the majority in any series, but the

significance of this chart shows that Type III injuries are more frequent than earlier represented.

Investigation of the location of levels of fracture of the ulna varied from that which only identified its frequency to most often in the upper third, but possibly to the junction of the middle and distal thirds, to the figures in Figure 1-3 taken from the same author twenty-nine years apart.

Study which sought to identify numbers or percentages of each type occurring in children revealed conflicting opinions. Type I varied from that of its being most often an injury of children⁴ to that of approximately equal frequency² in adults and children. Equal incidence was found in those studies^{3,2,5} which recorded actual numbers of children and adults in each

	Speed/Boyd 62 injuries	Bado 55 injuries	Bryan* 45 injuries
Type I	83 1/3%	60%	55.5%
Type II	10%	15%	13.3%
Type III	6 2/3%	20%	17.7%

*Does not equal 100% due to several lesions "not typable".

Figure 1 - 2

Speed/Boyd 1940	Boyd/Boals 1969
5%	19.5%
66 2/3%	71.0%
18 1/3%	8.2%
5%	1.3%
5%	12.0%

Olecranon at the level of the joint.

Junction of upper and middle third to olecranon.

Middle third.

Lower third.

Fracture of both bones with radial head dislocation (Type IV).

Figure 1 - 3

ACUTE MONTEGGIA LESIONS

type, and it is felt to be the more reliable value.

Type II was generally reported as an injury of the middle-aged, especially of women^{8,2} but several authors^{6,7} brought attention to the fact that children not only suffer from this type of injury but may also have associated posterior interosseus nerve injury.

Type III lesions are described as "confined to children"² and of approximately equal occurrence⁸ in children and adults. Figure 1-4 reflects these findings in acute

	Bryan ⁵	Bado ⁶
Type I	(11/25) 44%	(18/33) 55%
Type II	(0) 0%	(N/R) 0%
Type III	(5/8) 62%	(N/R) 100%

(/) = Total number children /
total number injuries

Figure 1 - 4

injuries of Types I and III. Type II incidence was not found in the literature.

MECHANISM OF INJURY

Speed and Boyd¹ reported that a direct blow over the posterior aspect of the proximal ulna produced this injury. However, in view of later knowledge, observations made in their report tend to disprove their hypothesis and are to be discussed.

Their hypothesis was accepted until 1949 when Evans⁸ used evidence gained from work with eighteen cadavers and clinical observation to support the thesis of hyperpronation as the mechanism of injury. Bado⁹ supported this theory of etiology as late as 1967. He used as evidence the statement that the bicipital tuberosity was most posterior in hyperpronation and that this position made the radius subject to greatest force from the biceps tendon when violent contraction

of this muscle occurred.

Both hypotheses were challenged in 1971 by Tompkins who presented convincing evidence that hyperextension with the forearm in neutral was the most acceptable mode of action for Type I injuries.¹⁰

This was based on the following data:

1. Radiological studies on normal subjects that identified the bicipital tuberosity most posterior in neutral rotation of the forearm, full pronation turning it laterally and supination turning it medially.

2. Clinical and radiological examination of acutely injured patients showing Type I Monteggia lesions having the forearm in neutral or slightly supinated.

3. The observation that in compound Type I fractures, the proximal ulnar fragment usually penetrates the volar skin on the ulnar side of the forearm, a phenomenon anatomically impossible if the forearm is in hyperpronation due to "blockage" by the radius.

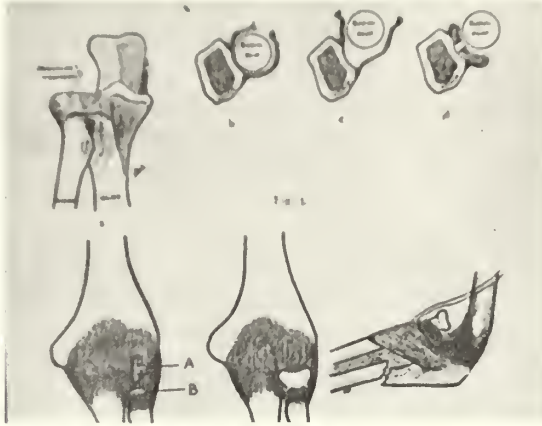
4. Type I lesions are usually transverse or comminuted with the butterfly comminuted fragment on the posterior aspect of the ulna. This is in contradistinction to Evans' work which only produced spiral fractures and then only in 2/3 of his cadavers. Watson-Jones, in his discussion of Evans' paper, felt that hyperpronation was an etiology only if spiral fractures were present but that another mechanism was present in transverse fractures. This comminuted posterior fragment suggests axial loading in hyperextension.

To these observations can be added several others concerning Type I lesions:

a. When dislocation of the radius occurs, it is caused by rupture of the annular ligament or a "pulling out" of the head of the radius from the annular ligament^{1,4} (Fig. 1-5).

b. Direct blows usually result in fracture of both bones, not a Monteggia lesion.¹

c. Biomechanical investigation of the moments of force and components of



force suggest, theoretically at least, that with the hand fixed and in pronation with the elbow in full extension or hyperextension, contraction of the biceps would tend to pull the head of the radius more securely into the lesser sigmoid notch. Neutral position of the forearm would tend to lift the radius out of the annulus.

All together, these findings would point toward a mechanism of injury of hyperextension of the elbow with the forearm in neutral or slight supination. Type II lesions are felt to be a variant of the mechanism which produces posterior dislocation of the elbow and most probably occurs in flexion. Type III lesions are felt to be a variant of Type I.

DIAGNOSIS

Any discussion of diagnosis of this injury must paraphrase the admonition of Speed and Boyd¹ that a fracture of the ulna with angulation or overriding without an accompanying fracture of the radius makes dislocation of the radial head suspect until proven otherwise. Such proof is obtained by including the elbow in all radiographs of suspected fractures of the ulna. The wrist should also be included to identify any radioulnar dislocation. Examinations of roentgens of the elbow show that extension of the longitudinal axis of the radius normally always passes through the center of the capitellum or its epiphysis in all anatomical positions⁴ (Fig. 1-6). Knowledge of this fact can help in questionable le-

sions, as can radiographs of the opposite elbow.

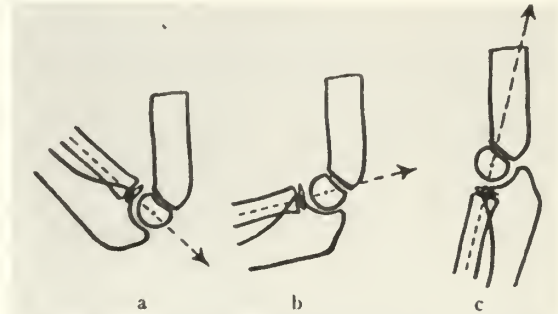


Fig. 1. Sketches of lateral views of bones at elbow in full flexion, midposition, and in full extension to demonstrate that longitudinal axis of radius normally passes through the center of the capitellar process or its epiphysis.

Awareness of the statistics already presented involving both bone fractures and radial head dislocations is also helpful.

In children, it is significant to realize presented involving both bone fractures are "greenstick,"¹¹ and this may be deceptive unless the elbow is included in the radiographic examination.

In addition to the above factors, a high index of suspicion is required as shall be shown under the discussion on complications.

TREATMENT

This discussion shall lend itself to the treatment of the acute lesion. As such, preferred treatment of these injuries in children universally consists of manipulation and immobilization in supination and flexion of 100 to 110 degrees. Almost all have excellent results as long as the radial head is kept properly reduced. Full supination is not required if the elbow is kept in 100 to 110 degrees flexion to keep the biceps relaxed. An exception to this method is the child with a Type II fracture in which the posterior dislocation of the radius is not stable when reduced in the flexed position.

Reduction is accomplished with the forearm in extension, providing gentle manipulation over the head of the radius while pronating and supinating the forearm. Once reduction of the radial head is felt to be complete, flex, extend, then flex

ACUTE MONTEGGIA LESIONS

	Type I	Type III	Not identified
Bryan ⁵	$\frac{3 \text{ opened}}{11 \text{ total}}$	$\frac{4 \text{ opened}}{5 \text{ total}}$	
Boyd, et al ⁸			$\frac{1 \text{ opened}}{20 \text{ total}}$
Smith ⁴			$\frac{7 \text{ opened}}{22 \text{ total}}$

Figure 1 - 7

No Type II's reported.

the elbow.⁴ If there is no interposition of the annulus, the radial head will remain reduced if the ulnar fragments are also reasonably reduced. In children, it is more important to reduce the radius accurately than to gain anatomic reduction of the ulna, as remodelling will correct minor angulation.

Indications for open reduction in children are related to the inability to adequately reduce the radial head or to keep it reduced once accomplished. Interposition of the annular ligament most frequently prevents reduction of the radial head. Interposition is of three types: (1) partial, in which portions of the ligament are interposed between the radial head and the ulna, (2) complete, in which the radial head "pulls out" of the ligament leaving it intact (this injury accounts for the majority of failures of reduction),⁴ and (3) fragmentary, in which osteo-cartilaginous fragments are present, most frequently associated with Type II lesions.

Internal fixation is recommended as described by Boyd et al, "plate" immobilization of the ulna after reduction of the radial head being preferable. Fascial loops are not indicated in the majority of patients.⁵ "Rod" fixation is acceptable treatment if a plate is not indicated.

Figure 1-7 represents the experience of several authors in open reduction of Monteggia lesions in children.

COMPLICATIONS

1. Chronic dislocation and malposition as a result of missed diagnosis is the most frequent complication, showing incidences of 23.7%,⁵ 51.7%,¹ and 16%⁴ in the various literature (Figure 1-8). Figure 1-8 represents results at one year of such a complication.



2. Recurrent dislocation of the radial head which probably can clinically be included with the above complication.

3. Posterior interosseus nerve neuropathy. This is most common in Type III but is reported in Types I³ and II⁶. Spontaneous recovery is expected in all cases,⁶ and exploration should not be attempted prior to six weeks post injury.

4. Fracture of the radial head in Type II.

5. Fracture of both bones with radial head dislocation. If the fractured radial head is displaced in a child, it should be reduced and kept in place as appropriate.

6. Distal radioulnar joint disturbance (not felt to be significant).⁵

7. Compound wounds.

8. Non-union, statistically small in children.

9. Myositis ossificans.

DISCUSSION

The Monteggia lesion in children has been presented to include definition, mechanism of action, incidence, diagnosis, treatment, and complications.

A Type I mechanism of injury is felt to be that of hyperextension while the forearm is in neutral or slightly supinated, and radiologic, clinical and biomechanical evidence have been used to establish that fact. Other types are described.

The incidence of each lesion in children was presented. Types I and III comprise approximately half of each type's total incidence, with Type I clearly the most frequent. Type II does occur, and when it does, it can be unstable with standard closed reduction.

Diagnosis consists of a high index of suspicion in all ulna fractures with particular attention being paid to "greenstick" injuries in children.

Treatment of choice is closed manipulation with immobilization in flexion of 100 to 110 degrees and supination. Open reduction is indicated in any lesion in which the radial head cannot be reduced or held reduced.

Complications have been discussed with the hope that further reductions of incidences of missed diagnoses can be accomplished.

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ADMISSION TO MEDICAL SCHOOL

THOMAS B. DUCKER, M.D.*

W. MARCUS NEWBERRY, M.D.**

The competition to enter the College of Medicine at the Medical University of South Carolina has stiffened remarkably in the last ten years. In part, this is a reflection of a national trend, where in 1963, there were over 14,000 applicants, and in 1973, there were over 36,000 applicants. This reflects a two and one-half fold increase in applicants, while at the same time, the places offered in medical school increased only one and one-half times. In 1963, at the Medical University of South Carolina, there were 196 applicants for 80 places in the freshman class of the College of Medicine. By 1973, there were nearly 1,100 applicants, a five and one-half fold increase. During the same period of time, the places for students entering the College of Medicine increased to 165, an expansion which represents twice as many physicians and is well over the national average.

There are many reasons for this dramatic increase in the number of applicants. In the 1950's, there was a great shortage of engineers, and people pursuing this type of education were guaranteed a position of good income immediately upon the completion of their college work. In the latter 1950's and early 1960's, there was a shortage of teachers and anyone completing his degree in this field was readily assured a job. In our race to the moon in the latter part of the 1960's, there was a shortage of scientists with graduate degrees to fill our need in these

highly scientific fields. In all of these fields, there are now sufficient professional persons who are qualified and appropriately educated. As we entered the 1970's, law schools across the nation had expanded to such a degree that there is now an overabundance in this profession. Thus, any person pursuing a formal education, graduate science, or law must face the reality that nearly one-third of such graduates will not find a position in their field.

In distinct contrast, the medical field still has a shortage. Although medical schools across the country have increased their student positions by over 50 per cent, and the Medical College at the Medical University of South Carolina has increased its positions over 100 per cent, planners at the federal level predict that the doctor shortage will continue through the 1970's. The medical field will be the last to become saturated simply because it takes, after a college degree, eight to ten years before an individual can practice medicine in his chosen field. This educational time is distinctly different from engineering or teaching wherein the person can immediately enter his field upon completion of undergraduate studies, while the graduate scientist and lawyer require an additional three years of study after a college degree. In the interim, the shortage of physicians and the opportunities in this field are apparent to all. Consequently, there has been a massive increase in the number of applicants for admission to medical school.

To meet the present physician shortage, the Medical University of South Carolina expanded significantly over the last ten years. In the process, faculty positions increased three times, and the postgradu-

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ate special medical programs doubled. More highly qualified professional people with a wide range of medical abilities expanded the professional disciplines that contribute to a formal medical education. With this growth came an improved reputation for the College of Medicine and South Carolina applicants who previously sought their education out of the state now have turned to their own state-supported institution. For this reason, for the first time in the history of the College of Medicine, there is an abundance of qualified individuals seeking application to the College of Medicine.

Not only is there a change in professional opportunities, but also there is a change in applicant composition for the professional degree. Traditionally, the South Carolina physician population has consisted predominately of white males. Lately, the applicant pool has changed remarkably. For example, women competing for medical school have increased nine times in the last ten years and now make up a substantial portion in our classes. A similar trend is noted for black applicants. All these collective factors make applicant competition very keen.

SELECTION

In the last few years, the selection of students for admission to the College of Medicine has become an increasingly arduous task. Despite intense research by many medical schools across the country, those factors or personal qualities which determine the best physician are not clearly outlined. The members of the Admissions Committee for the College of Medicine at the Medical University of South Carolina feel relatively secure in determining the good student who will survive the difficult basic science curriculum; however, the final determination of ascertaining those who will make the best clinical physicians is difficult for even the most industrious and honest committee member. As pointed out by Rhoades, et al.,⁴ "There is little objective evidence available to make accurate pre-

dictions about the medical student's performance in clinical courses." Evaluation of their data can only conclude that—given certain standards of intelligence, premedical preparation, adequate admission test performance, acceptable recommendations, and a reasonable range of activities—motivation best determines a medical student's performance, especially in his clinical years. Yet no person or persons have come up with a formula to ascertain motivation. Consequently, the acceptance still depends primarily on academic ability.

As the whole issue of selection has become more critical, professional educators have addressed themselves to the problem. It is agreed that fine scientists often make good medical doctors, but there are many more physicians whose records indicate that they were not superior scientists and instead were highly-motivated individuals. Consequently, there have been a number of suggestions to improve the selection process. For example, Kimball³ advocated an open admission policy, but conceded that chaos and confusion would follow in the teaching of huge classes, particularly in the introduction of students to patients. Funkenstein² supported a political solution to the problem, wherein a representative class would be built both from superior applicants and by lottery. These suggestions have achieved little support.

In most European countries, large numbers of students are allowed to enter medical school at an age and educational equivalent that correspond to the American junior year of college. The European medical education usually takes six years, with the first four years corresponding to our premedical sciences of college and basic sciences of the first two years of medical school. After these four years, there are strict examinations and only those students who have clearly qualified in the basic sciences are allowed to enter into the clinical years. In effect, this does not achieve a more open admission policy

ADMISSION TO MEDICAL SCHOOL

but delays the selection process and places full reliance upon an objective examination covering the basic sciences. This makes the admissions process easier for the medical schools but removes from consideration any qualities other than the ability to master the basic sciences. In addition, unsuccessful applicants find that they have invested several years of study and expense without achieving any career goal. A similar situation is seen in our system with unsuccessful applicants who are not well advised or do not heed good advice and obtain unwanted graduate degrees in an attempt to gain admission to medical school.

An imaginative solution to the selection problem, as clearly stated by Rhoades, et al., suggested a clinical trial in the undergraduate years. If such a clinical trial, like that possible in nursing degree programs, were to be added to the admissions requirements, then the admissions committees could evaluate both basic science and clinical aptitude. Perhaps undergraduate medical education should be drastically rearranged so that it included liberal arts, basic science, and clinical application of nursing or of physicians' assistants. From this undergraduate school, the most outstanding individuals could be accepted into the College of Medicine and work towards a doctor's degree. This form of premedicine training would provide more information for selection by medical school admissions committees, decrease the shortage of nurses, and assure unsuccessful medical school applicants a useful education.

Meanwhile, there has been no great basic change in the admissions policies of medical schools in the United States. We continue to judge the best applicants to be those students who have performed well in college, who have scored well on national testing, and who seem sincere, motivated, and level-headed in their interviews.

APPLICANT EVALUATION

Each applicant to the College of Medi-

cine is carefully evaluated. The Admissions Committee acts on each individual separately after discussing his or her credentials. These credentials are used to derive an overall profile of each candidate.

An accumulative grade point average of all recognized academic courses in college is mathematically determined. If an "A" is a 4, a "B" is a 3, a "C" is a 2, then the applicant must have approximately a 3.3, or a high "B" average, to be competitive in the field. This grade point average has steadily climbed in the last five years so that it is no longer possible for the "C+" to "B—" student to be a serious applicant. This fact comes as a shock to many. However, the Committee has to look favorably upon those candidates with outstanding academic records and certainly cannot discriminate against such tangible results. Obviously, students have to demonstrate a proficiency in academic work or they cannot be expected to perform well in the rigorous curriculum of medical school. A sick patient has little need for a likeable doctor who was not able to master the science of medicine.

The grade point average alone will not stand as a magic number to gain acceptance. The grades themselves are further evaluated. The trend in the student's performance is equally important. A student who did extremely well in his freshman year but was a poor student by his junior year is not the same serious contender as the student who started off poorly and comes to the Admissions Committee with a very good recent performance. In addition, we evaluate carefully the more difficult science courses in college because these are often our best indicator of the student's performance in the basic sciences during his early months in the College of Medicine.

For national evaluation, there is the Medical College Admission Test which is a requirement for all applicants to the College of Medicine. The applicant may

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take the test more than one time, and his best score will be considered by the Admissions Committee. This admission test aids the Committee in evaluating the student's educational background. Applicants whose total scores are below 2,000, or in the lower one-third of the nation, are not favorably considered. Further analysis has shown that performance on the science section of this test correlates with performance in the basic sciences of the College of Medicine.

There is now sufficient evidence that college grades have changed gradually over the last twenty years. Honors from a major university's undergraduate college could be achieved with a 3.5 scholastic average in the 1950's; now it is nearly 4.0. A few schools have allowed their grades to be higher in order to assure their students a place in the graduate school of their choice. Such complex changes force admissions committees to rely more on the national Medical College Admission Test as an assessment of academic ability.

The applicant's recommendations from his undergraduate college are an important consideration by the Admissions Committee. The outstanding college student is readily recognized by his professors. The low-average student, on the other hand, achieves little recognition and has less personal contact with his professors. These recommendations which are based upon personal observation of student performance constitute meaningful individual evaluations.

A reasonable range of extracurricular activities is expected of each applicant. These reflect a student's interests, motivations, and his involvement with the society around him. Such activities can also provide insight into a student's capacity for work.

Once these factors are in the applicant's file, and if he is deemed competitive, interviews are arranged with members of the faculty of the College of Medicine. The interviewers come from both

sides of medical education, basic sciences and clinical sciences. In this interview, the faculty member will try to find out why the applicant is interested in the study of medicine and why he wishes to attend the Medical University of South Carolina. At the same time, any limitations or liabilities—emotional, physical, or personal—which would significantly hinder or handicap his performance as a physician are ascertained. The applicants are asked to describe any additional experiences or endeavors in special projects that would bring out their abilities. Often they are asked to describe their extracurricular activities, both during the school year and during intervening summers. Finally, and most importantly, the student's motivation to succeed in the College of Medicine is openly discussed. From each interview, a summary is written and the applicant is scored in the opinion of the interviewer as to acceptability to medical school.

In-state residents are given preference profile positions. This policy will continue until all other states stop discriminating against the South Carolina applicants. A few outstanding out-of-state applicants, especially those with definite South Carolina ties, are accepted each year. Though the out-of-state applicant pool is definitely very limited, it is sufficient to build the broad cross-section needed for a fine College of Medicine.

Finally, to round out the student body, small additional criteria are put in the admission process to make "certain" allowances for the economic and social background of select students.¹ Basically, this means that the minority student must obtain the same grade point averages, recommendations, and interview assessments that all other applicants must obtain, but, on occasion, their Medical College Admission Test scores may not be as competitive because of the select education that they received in their younger years.

APPLICANT REJECTION

Obviously, many, many applicants fail

ADMISSION TO MEDICAL SCHOOL

to gain acceptance into the College of Medicine. In the vast majority of cases, even if the applicant applies again, his credentials will not be sufficient for him to gain admission. Many such applicants are truly motivated and some enter graduate school. In the process, they can improve their overall grade point average, the trend of their academic performance, and their ability to perform on the Medical College Admission Test. At the same time, they usually become more involved with their professors and their recommendations improve. In the majority of cases, this additional education has not erased the earlier academic performance as an undergraduate student, but some applicants have gained their place in the College of Medicine and have done well. It is required that they obtain their graduate degree prior to admission to medical school.

Generally speaking, the members of the Admissions Committee are reluctant to make concrete suggestions to applicants that fail to gain acceptance. Specifically, in the last five years, the overall grade point average of the typical student entering the College of Medicine has climbed by at least one-tenth of a point each year. Consequently, a student who fails to gain acceptance will work to improve his grade point average only to just miss arriving at that acceptable level wherein he is a truly competitive candidate.

The policies of our school are no different than those of other good medical colleges. Our students, once matriculated and educated must compete on a national level to be licensed and accepted for residency positions. With the current pressures

from the federal government, the standards of national licensing examinations are going to become more stringent. Consequently, it is essential that our students begin their medical studies on an equal footing with their peers throughout the nation in order for their education to proceed on schedule.

The fact that many rejected applicants could contribute significantly to the health care constitutes one of the basic challenges to medical educators. Perhaps a reasonable solution would be to revamp the undergraduate premedical education.

CONCLUSION

The selection process for applicants into the College of Medicine continues to be a trying task. Currently, the College of Medicine at the Medical University of South Carolina has one of its best student bodies. There is little doubt in the opinion of the Admissions Committee that the majority of these students will make good physicians. History and time have proven that the current admissions process is indeed an effective way of selecting individuals to enter medical school. Until it can be proven otherwise and/or until undergraduate health science education changes, the selection of students will continue to follow the guidelines as stated in this article. The applicant's evaluation and his eventual success in medical school cannot be wholly predicted; however, over 90 per cent of those who gain admission do complete their course of study and are practicing doctors performing in an admirable way. It is true that an intangible factor, termed "motivation," is the single most important quality that finally determines the real leaders in medicine.

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HYSTEROSCOPY

W. B. NORMENT, M.D.*

The technique of hysteroscopy is a fairly simple procedure, particularly with the modern instruments of today. Many previous reports have been made in regard to the different media used in hysteroscopy, and not too much has been published as to the exact technique. The object of this paper is to deal more with the technique of hysteroscopy so that anyone can do this procedure with very little difficulty. Previous publications of the different media should be reviewed. Carbon dioxide is used by investigators in West Germany; however, there is some danger associated with this gas, since the endometrium absorbs carbon dioxide much more rapidly than the peritoneum does. So, carbon dioxide probably should never be used for hysteroscopic examination (unless monitored with the "hystero-flator-1000"). Dextran 10 per cent has also been used as a medium in the past and still is used to some extent. The objection to Dextran 10 per cent is that blood mixes with the Dextran and sometimes prevents a clear vision. Five per cent Glucose in water has been used by some investigators, however, it does not stop bleeding in the uterine canal and the smallest amount of blood in the canal will prevent, with 5 per cent Glucose, clear vision at times. We use Cytal with suction hysteroscope. The value of suction is that the fluid, Cytal, runs into the uterine cavity and is immediately sucked out by the suction equipment, similar to the action of gastric suction equipment, and in this way, even if the patient is bleeding, very little blood is seen. The mucosa is very clearly outlined. The os of

the cornu can be seen easily, and, with the lens systems that are used today, the hysteroscope can be brought just inside the internal os and the entire uterine cavity can be observed if suction is employed. This will be discussed later in detail.

Description of Hysteroscope: A Hopkins lens is employed which has an extremely wide angle view, so that the entire uterine canal can be seen at one time without any rotation of the instrument. Also, in this country, a Foroblique lens system is made for hysteroscopes which is also of value. The lens system we use is made in West Germany. It is a forward-vision lens system which has been very successful in our hands.

Fibro-optic light, which is an arc light, is employed as a light source. This light is transmitted through a six foot fiberoptic cord and is very brilliant. The light is strong enough for photography at 1/25th of a second if a still photograph is desired.

The sheath that incorporates the lens system, together with a small channel for the Cytal to run into the uterine canal, the small channel is incorporated in the sheath.

On either side of the intake of Cytal, there is a small outlet on either side of the intake. Rubber tubing is attached to the two openings or outlets for the reflux of fluid and these are attached to suction on both sides, so that the Cytal runs in the small metal tube, into the uterine cavity and refluxes back around and is sucked out by suction around the lens system and the tubing as described above. The exchange of Cytal is so rapid, that even with the patient bleeding, a very clear vision can be obtained.

*Greensboro, N. C.
Certificate of Merit Award, 1950 by American Medical Association

HYSTEROSCOPY

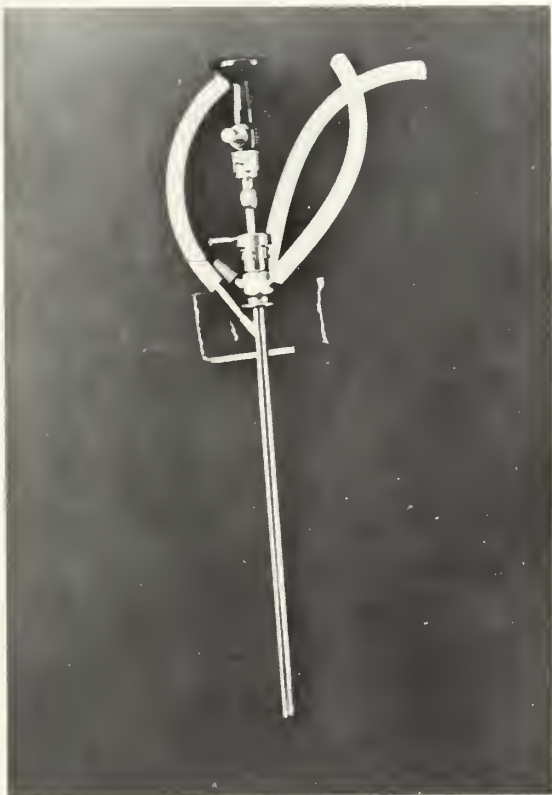
We believe that the greatest advantage of this suction device is that, practically always, a clear vision can be obtained and there is not a question of a good or bad viewing. With the fibro-optic light as described above, together with the suction apparatus which is very important, it makes hysteroscopy a fairly simple procedure. With the instrument just inside the internal os, with the Cytal making a rapid exchange, the entire uterine cavity can be observed together with the cornu and oftentimes the openings of the fallopian tubes.

The purpose of a hysteroscopic examination is manifold, mainly, of course, to detect whether an endometrial polyp or submucosal fibroid is present. It is certainly, in itself, not diagnostic of a malignancy of the endometrium. Oftentimes, the curet will miss these endometrial polyps and submucosal fibroids. Also, with a palpable serosal fibroid, if on hysteroscopic examination the fibroid

does not protrude into the uterine canal, then we can assume that the fibroid has nothing to do with uterine bleeding, and this way many hysterectomies may be avoided.

At times, it becomes necessary to stop the suction device by clamping the suction tubes and allowing hydraulic pressure from the container of Cytal to dilate the uterine canal. This is of aid in two respects, in that the hydraulic pressure tends to stop bleeding, and also a better view of the uterine canal can be obtained. The stopping of the suction device is only for a few seconds, and then it is resumed in the usual manner. A view of the opening of the fallopian tubes is better ascertained when the suction is cut off and the hydraulic pressure of the Cytal is used.

Technique of a Hysteroscopic Examination: The patient is under Pentothal and gas anesthesia and the vaginal mucosa and cervix prepared in the usual manner, similar to a D&C. Drapes are applied. A tenaculum grasps the upper lip of the cervix and the cervix is dilated slowly with Hegar sounds. Later, a Goodell dilator can be used, if necessary. Following the dilation of the cervical canal, the sheath is inserted, the obturator removed, and the lens system is inserted and connected up to the light source. Then the Cytal is allowed to flow for a few seconds. Uterine canal is usually seen without any difficulty. Since the uterine canal is shaped like an inverted triangle, examination of both cornu is usually a simple matter. Fulguration of the openings of the fallopian tubes is not adequate for occlusion since they will re-cannulize in many cases. Also, there have been some reports of burning of the intestinal tract when fulguration is attempted in this manner. Unless the musculature of the fallopian tube is incorporated in the fulguration, then the fulguration is not a safe procedure for sterility. If only the mucosa is fulgurated, it is not of much value. The hysteroscope should be kept at least one inch away from the endometrium



Hysteroscope with suction outlets.

HYSTEROSCOPY

since there is a blurring of vision if the lens system is too close to the endometrium.

Photography of the uterine canal may be made with a 35-mm reflex camera or a 16-mm motion picture camera. With the very bright light source, usually good results are obtained in photography.

A hystero-gram or x-ray film of the uterine canal is not accurate at times. Oftentimes, there is a filling defect, which is piling up of the endometrium and not a true tumor. The object of the hysteroscope is to help determine which patient needs a hysterectomy and which does not. Often, a small uterus will have a sub-mucosal fibroid. On the other hand, a serosal fibroid may not protrude into the uterine canal and the patient does not need a hysterectomy.

Discussion by D. S. Pope, M.D., Columbia, S. C.

Dr. Norment deserves much credit for his continuing efforts to improve the technique and results in hysteroscopy. I have followed his work since he read a paper before the Medical Society of Richland County in Columbia, S. C. in 1955.

The incorporation of fiber-optic lighting was a major improvement, and now the use of suction with a different medium, Cytal, gives much better view of the path-

ology.

Several young research gynecologists have employed hysteroscopy in their clinics and it is an ever expanding field of interest.

Dr. Valle emphasized the value of hysteroscopy in selecting biopsy sites, searching for bleeding sites and searching for congenital defects in utero.

Rioux also stressed the value of the use of the hysteroscope in locating IUD's and uterine pathology such as polyps and sub-mucous fibroids. Rioux also advocated a team to do simultaneous laparoscopy and hysteroscopy. The operator of the laparoscope acts as a monitor to prevent bowel burns by the hysteroscope and to monitor against tubal damage when the operator is working through the uterine tubal opening inside the cornu and in the proximal portion of the tube.

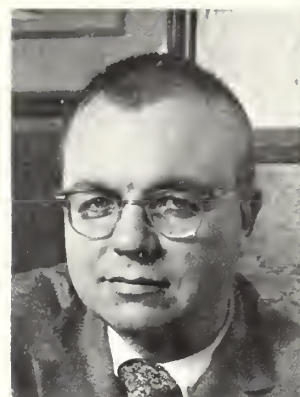
Cunanan and others advocate paracervical block for hysteroscopy.

Mohr points out that hysteroscopic uterine tubal coagulation for sterilization purposes is a 10-minute procedure done under paracervical infiltration and that the patient should not be required to spend more than 2 hours in the clinic and this is a much simpler procedure than laparoscopy.

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President's Pages



Rural Health Delivery—An Impossible Dream?

The shortage of physicians—particularly those in rural areas—continues to be a major source of the problems facing the medical profession today. In an attempt to give professional direction towards solving this problem I proposed a rural health delivery system to the House of Delegates of the South Carolina Medical Association last December, and it was adopted unanimously. Information about this plan was furnished to legislators, hospitals, foundations, and all other people interested in this problem. On January 17th, I appeared before our U.S. Representatives and Senators to inform them of this program and request funding from HEW and HUD where feasible. I have appointed a committee with myself as chairman to include Drs. Harold Hope, Gavin Appleby, Joseph Flowers, Jim Barnett, Harrison Peeples, Waitus Tanner, Charles Wyatt, and Hal Jameson. This committee met on February 6th, to consider the broad details of the plan. It was the consensus of the group that guidelines should include at least 3,000 people in the medical service area to support one private physician's office. Because of the inherent disadvantages of solo practice involving coverage, that generally speaking, the plan would attempt to establish an office staffed by at least two physicians requiring approximately 6,000 people in a medical service area within about a 20-mile radius. It was also agreed that no physician should be put in an area where adequate hospital facilities were not within a reasonable traveling distance. Facilities and equipment available to the physicians included in this program must be as modern as the physicians training. The committee also approved retaining American Health Systems Inc. in developing feasibility study when feasibility money becomes available.

The main problem remains the financing of the feasibility study which is estimated to cost approximately \$50,000. So far we have only had pledges of \$4,500 from the South Carolina Farm Bureau Federation and the National Bank of South Carolina. Negotiations are under way to obtain funding from the Duke Foundation and the Self Foundation in conjunction with the South Carolina Hospital Association. Approximately 40 other foundations have been approached, but because of unfavorable financial conditions or previous commitments, they have been unable to provide any money. A possible later source of help is the Rural Health Care Delivery Act of 1975 (HR5236). This would establish an Office of Rural Health within HEW and would assist in the development of rural health care delivery models and components. However, I think it is time that we doctors took the leadership in providing funds to get this feasibility study off the ground. Some of the people we approached have already asked how much the doctors are contributing. Of course, we are contributing our time and expertise to a

considerable degree. However, I would like for the SCMA to be able to show other people that we intend to put our money where our mouth is. I have already written to the county medical associations asking for contributions to help get this feasibility study off the ground with a goal of \$15,000. This money may be contributed to the tax exempt South Carolina Medical Education and Research Foundation. I would like to appeal to every member of the SCMA to add his contribution toward this goal as soon as possible. If the South Carolina Medical Association can solve this problem, it will demonstrate louder than any other action that we doctors are interested in providing health care for all people. Years ago as a child I was told the story of the little red hen. She tried to interest the various animals in the barnyard to help her plant the wheat. No one volunteered. She asked for help harvesting the wheat; no one volunteered. She asked for help in grinding it into flour, and no one volunteered. She asked for help baking the bread; no one volunteered. Finally, when the bread was baked, everyone certainly volunteered to help her eat it. After being turned down by all these agencies, I feel a little bit like the little red hen, but if we raise the money and do this job, we can be absolutely sure that: 1) it will be satisfactory to both patient and doctor, 2) it will minimize third party interference, 3) it will show that doctors can and should provide leadership in solving health problems. Please support your RHDS committee with your advice and your money!

Donald G. Kilgore, Jr., M.D., President
South Carolina Medical Association



50 YEARS AGO

April 1925

The editorial pages were given over to the description of the hospitals of Spartanburg in anticipation of the annual convention of the Association. It noted that the State Association would launch a pioneer movement for this state in the matter of periodic health examinations.

Editorials

Getting People in Med School in South Carolina

Ducker and Newberry have made a valuable contribution to South Carolina medicine by presenting in their article in this issue of *The Journal* the considerations used in selecting the future physicians for our state. The standards used in selecting the chosen few from all the many applicants to Medical School are obviously important to the 1,100 people applying to MUSC in 1973, but also are important to all South Carolinians because the results of the selection process will determine the quality of the physicians in South Carolina in the future. It is reassuring to learn of the great care and conscientiousness used by the selectors. It also is comforting to know that political influence has little to do with determining who will be admitted to Medical School and therefore who will be doing the operating and the medicating on South Carolinians in the next decade. This is particularly good news in view of the fact that the trustees of our state Law School have just opened the way for possible political admissions to that great institution.

It looks like the Medical School admissions committee is being very scientific and liturgical about the admissions process, but it all boils down to two stories I remember from my college days being true. This was in the very early days of motivational and performance research. One of the giant corporations invested much time, effort, and money in devising a scheme to predict which of their beginning employees would turn out to be their most valuable and successful executives. All their effort and research indicated that the most reliable factor in predicting

success was simply the college grades made. Also, at about that time, the Army went through exhaustive physiological, psychological, mental, etc., tests in an effort to determine which soldiers would function best in the tropics and which would function best in the arctic. As it turned out, the most accurate method was simply to ask the soldier whether he liked cold weather or hot weather better. This is apparently about what the Medical School admission policy is: to get the best students possible and then try to find out which ones really want to be doctors. I can imagine no better way!

Consideration of the selection process in its full scope brings to mind a couple of problems. Although not as great as in the European medical education system, there appears to be a substantial number of South Carolinians who have staked their future on getting into medical school but cannot. I personally know several of these unfortunates and it is truly heart-rending. Figures in Ducker and Newberry's article suggest there may be as many as 900 of these people each year in South Carolina. This is an enormous pool of great talent, with great interest in medicine and probably considerable potential. I wish someone could concoct a way to utilize this resource for its own and for everyone's benefit. Also, it would be helpful to contrive a method to eliminate some of the more hopeless candidates before they have completed college and, in many cases graduate school, with no place to go from there except medical school and with no chance of going there. But that is probably impossible in our free society, and as long as "hope springs eternal in the human breast."

EEK

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Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

Contraindications: Glaucoma, obstructive disease of the gastrointestinal tract, obstructive uropathy, intestinal atony, toxic megacolon, hiatal hernia associated with reflux esophagitis, or unstable cardiovascular adjustment in acute hemorrhage.

Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

Overdosage may cause a curare-like action, with loss of voluntary muscle control.

For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and this possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evidenced by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

SEARLE

Searle & Co.

San Juan, Puerto Rico 00936

Address medical inquiries to: G. D. Searle & Co.
Medical Department, Box 5110, Chicago, Ill. 60680 481

"Antiacid" action for ulcer patients...

one of the many things you need in an anticholinergic.



Pro-Banthine is considered adjunctive in total peptic ulcer therapy that may include diet, conventional antacids, bed rest, and other supportive measures.

Pro-Banthine is provided in several different dosage forms which will meet virtually any clinical need. It is just as versatile in filling patient needs, among which are:

"Antiacid" action — Pro-Banthine® (propantheline bromide) reduces gastric secretory volume and resting total and free acid.

"Analgesic" action — Pro-Banthine helps to control the acid-spasm-pain complex.

Vigorous anticholinergic action — Pro-Banthine® Vials, 30 mg., are for intramuscular or intravenous use when prompt and vigorous anticholinergic action is required.

Mild anticholinergic action — Pro-Banthine® Half Strength, 7.5 mg. tablets, for more exact adjustment of maintenance dosage in mild to moderate gastrointestinal disorders.

Pro-Banthine® (propantheline bromide)

a good
option
in peptic
ulcer

PAIN RELIEF FOR THE MAJORITY

NO.4—for pain intensity below the need for injectables

As a rule, only pain that requires morphine is beyond the scope of Empirin® Compound with Codeine No. 4. That's because it delivers a full grain of codeine. (In the preferred phosphate form.) Its antitussive action is particularly appreciated by patients with fractured ribs, and following chest or abdominal surgery. Its low addiction liability is a bonus for all patients who require potent analgesia.

NO.3—for almost all other kinds of lesser pain

Most other kinds of lesser pain respond to Empirin Compound with Codeine No. 3—whether musculoskeletal, neurological, soft-tissue or visceral. One might say No. 3 is an "all-purpose" analgesic — not too little, not too much. Just right for your out-patients in these categories.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

BURNS

Wherever it hurts

EMPIRIN® COMPOUND \bar{c} CODEINE

No.3, codeine phosphate*(32.4 mg) gr $\frac{1}{2}$ · No.4, codeine phosphate*(64.8 mg) gr 1

*Warning — may be habit-forming.

Each tablet also contains aspirin gr $3\frac{1}{2}$, phenacetin gr $2\frac{1}{2}$, caffeine gr $\frac{1}{2}$.

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities.

Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F CO.
Carolina, P.R. 00630
Subsidiary of
SmithKline Corporation

KEEP THE HYPERTENSIVE PATIENT ON THERAPY KEEP THERAPY SIMPLE WITH **DYAZIDE**[®]

Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

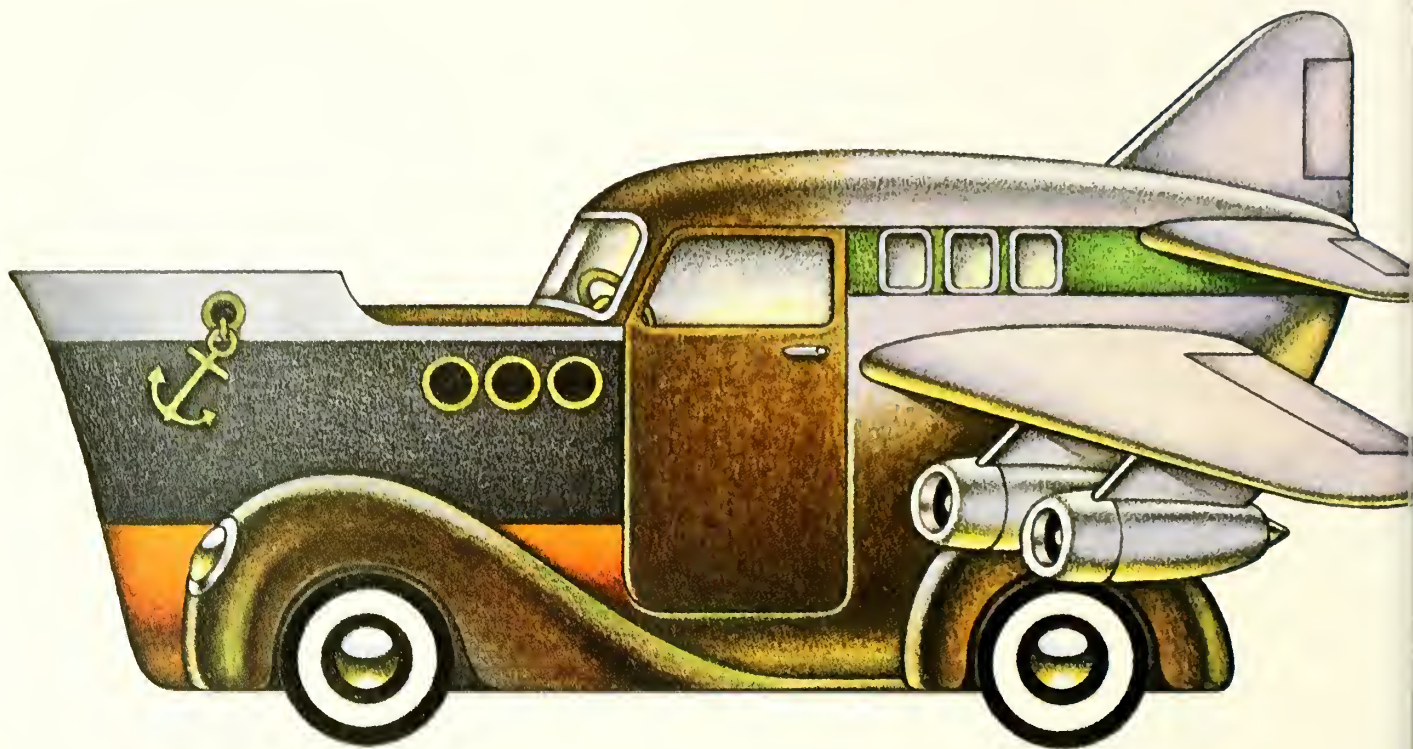
Trademark

Neither inconvenient potassium supplements
nor special K⁺ rich diets needed as a rule.
Just 'Dyazide' once or twice daily for maintenance.



Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP



On land, sea, and in the air...

Up to 24 hours of effective control with a single dose...in nausea, vomiting and dizziness associated with motion sickness.

Dosage: 25 to 50 mg. 1 hour before travel.

Available on prescription only.

BRIEF SUMMARY OF PRESCRIBING INFORMATION
CONTRAINDICATIONS. Administration of Antivert during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did

not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

ROERIG 
 A division of Pfizer Pharmaceuticals
 New York, New York 10017

Antivert®/25 Chewable Tablets
 (meclizine HCl) 25 mg.
 for motion sickness

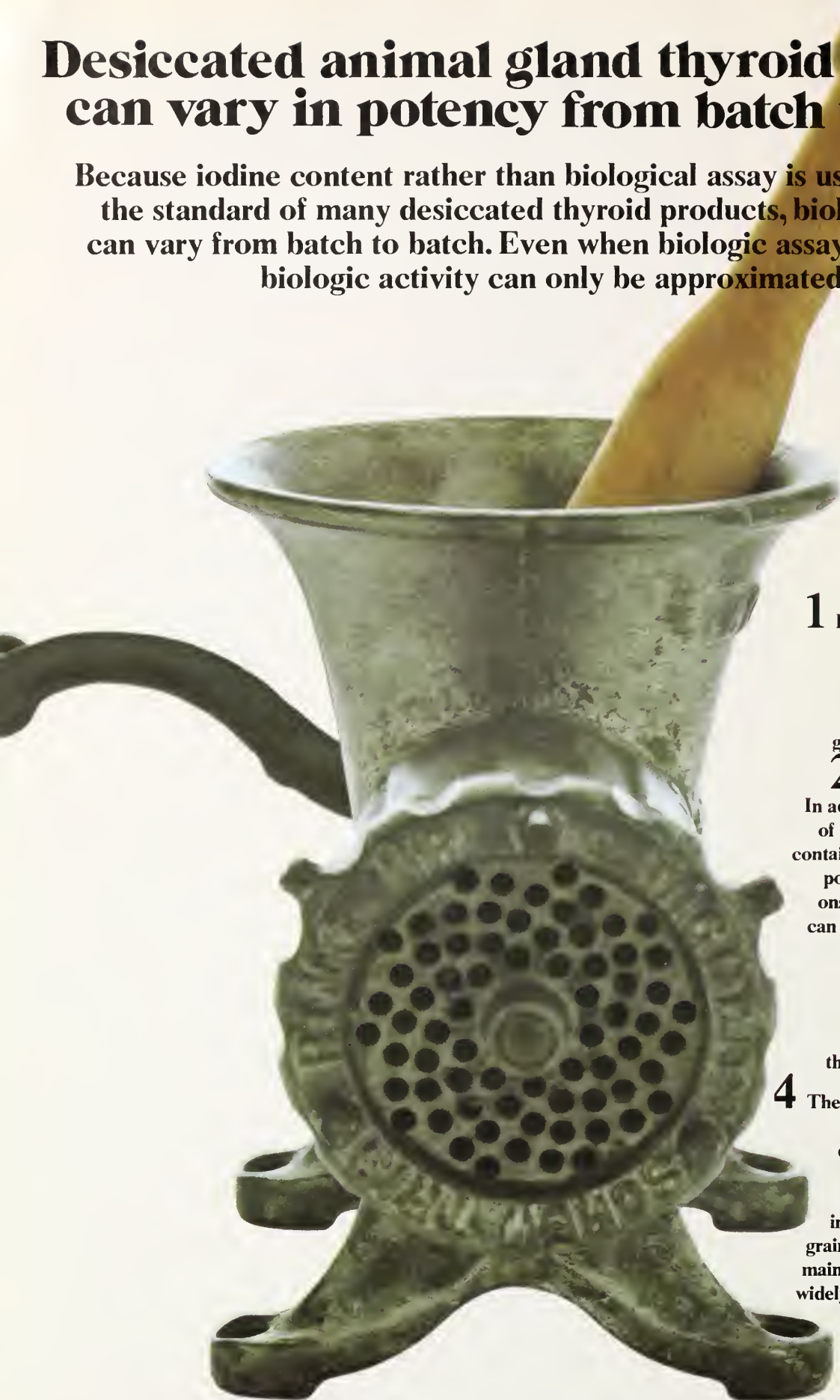
Synthroid[®]

(sodium levothyroxine, U.S.P.) FLINT



Desiccated animal gland thyroid products can vary in potency from batch to batch.

Because iodine content rather than biological assay is used to measure the standard of many desiccated thyroid products, biologic activity can vary from batch to batch. Even when biologic assay is employed, biologic activity can only be approximated.



1 It is recognized that T₄ and T₃ content in desiccated thyroid and thyroglobulin varies from animal to animal, by animal species, geography, and animal diet.

2 Of therapeutic concern: In addition to varying amounts of T₄, desiccated thyroid may contain varying amounts of T₃, a potent compound with rapid onset and fleeting action that can produce metabolic surges.

3 Even when kept under proper storage conditions, desiccated thyroid deteriorates more rapidly than the synthetic hormone.

4 The "usual maintenance dose" for the widely prescribed desiccated thyroid is "from 1 grain to 3 grains per day, but it may vary, in individual patients from 1/2 grain to 10 grains."¹ The "usual maintenance dose" of the most widely prescribed thyroglobulin (which is also a desiccated thyroid product) is "0.5 to 3.0 grains daily."²

1. Armour Thyroid (Tablets), 1975 Physicians' Desk Reference, p. 561.
2. Proloid® (thyroglobulin), 1975 Physicians' Desk Reference, p. 1575.



Every batch of Synthroid® T₄ is of controlled potency. (sodium levothyroxine, U.S.P.) FLINT

SYNTHROID is T₄. It provides your patients with everything they need for complete thyroid replacement therapy.

1 Sodium levothyroxine is *not derived* from any animal gland source. It is a synthetic and, since sodium levothyroxine is the only active ingredient, its weight is the sole determinate of potency.

2 SYNTHROID (sodium levothyroxine) is T₄ which is converted by the patient to T₃ at the cellular level, thereby providing a physiologic source and amount of T₃ to meet metabolic needs for complete thyroid replacement therapy. Because the onset of effect is slower and more steady, the possibility of sudden metabolic surges is reduced with SYNTHROID therapy.

3 SYNTHROID (sodium levothyroxine) products have a longer and more reliable shelf life than Thyroid U.S.P. when kept under the same proper storage conditions. There is no animal protein present in SYNTHROID products.

4 A recent study of 44 patients with hypothyroidism indicates that 89 percent of the patients were maintained with doses of L-thyroxine (SYNTHROID) between 100 mcg. and 200 mcg. (0.1 mg. and 0.2 mg.) per day.³

3. Stock, J.M., Surks, M.I., and Oppenheimer, J.H.: Replacement dosage of L-thyroxine in hypothyroidism. A re-evaluation. New Engl. J. Med. 290:529-33, 1974.

**Eliminates many
of the uncertainties of
desiccated thyroid therapy.**

Synthroid®
(sodium levothyroxine, U.S.P.) FLINT



FLINT LABORATORIES
DIVISION OF TRAVENOL LABORATORIES, INC.
Deerfield, Illinois 60015

See reverse side for full prescribing information.

Synthroid[®]

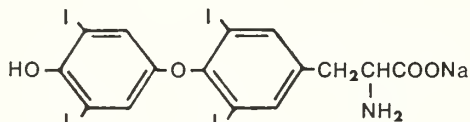
(sodium levothyroxine, U.S.P.*) FLINT

Synthroid Tablets—for oral administration
Synthroid for Injection—for parenteral administration



Description

SYNTHROID (sodium levothyroxine) **Tablets** and SYNTHROID **Injection** contain synthetic crystalline sodium levothyroxine (L-thyroxine). L-thyroxine is the principal hormone secreted by the normal thyroid gland.



Sodium Levothyroxine

Actions

SYNTHROID (sodium levothyroxine) **Tablets**, taken orally, provide hormone that is readily absorbed from the gastrointestinal tract. SYNTHROID **Injection** is effective by any parenteral route. Following absorption, the synthetic L-thyroxine provided by SYNTHROID products cannot be distinguished from L-thyroxine that is endogenously secreted. Each is bound to the same serum proteins and each exhibits a six to seven day circulating half-life in the euthyroid individual.

Both SYNTHROID products will provide L-thyroxine as a substrate for physiologic deiodination to L-triiodothyronine. Therefore, patients taking SYNTHROID products will demonstrate normal blood levels of L-triiodothyronine even when the thyroid gland has been surgically removed or destroyed by radioiodine. Administration of levothyroxine alone will result in complete physiologic thyroid replacement.

Indications

SYNTHROID (sodium levothyroxine) products serve as specific replacement therapy for reduced or absent thyroid function of any etiology. SYNTHROID **Injection** can be used intravenously whenever a rapid onset of effect is critical, and either intravenously or intramuscularly in hypothyroid patients when the oral route is precluded for long periods of time.

Contraindications

There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis. (See WARNINGS)

Warnings

Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions

Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule. With SYNTHROID (sodium levothyroxine) **Tablets**, the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

Adverse reactions

Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration

For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0.2 mg) of SYNTHROID (sodium levothyroxine) **Tablets** daily will restore normal thyroid function and only occasionally will patients require larger doses. Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism, special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent onset of hypothyroidism, full replacement dose of 150 mcg (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view of the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patient as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedematous infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 mcg (0.025 mg) per day. Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at three to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration. Laboratory tests to monitor thyroid replacement therapy are of limited value.

Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with the clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occurs and should not be considered evidence of overdose per se.

In all cases, clinical impression of the well-being of the patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critical importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size, the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROID **Injection** may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsiveness within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred. Like the oral dosage form, SYNTHROID **Injection** produces a predictable increase in the circulating level of hormone with a long half-time. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient is fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

SYNTHROID **Injection** by intravenous or intramuscular routes can be substituted for the oral dosage form when ingestion of SYNTHROID **Tablets** is precluded for long periods of time.

How supplied

SYNTHROID (sodium levothyroxine) **Tablets** are supplied as scored, color-coded compressed tablets in 6 concentrations: 25 mcg (0.025 mg)—orange . . . 50 mcg (0.05 mg)—white . . . 100 mcg (0.1 mg)—yellow . . . 150 mcg (0.15 mg)—violet . . . 200 mcg (0.2 mg)—pink . . . 300 mcg (0.3 mg)—green. Depending on strength, these tablets are available in bottles of 100, 500, 1000 and 5000.

SYNTHROID (sodium levothyroxine) for **Injection** is supplied in 10 ml vials containing 500 mcg of lyophilized active ingredient and 10 mg of Mannitol, U.S.P. A separate 5 ml vial containing Sodium Chloride Injection, U.S.P. is provided as a diluent.

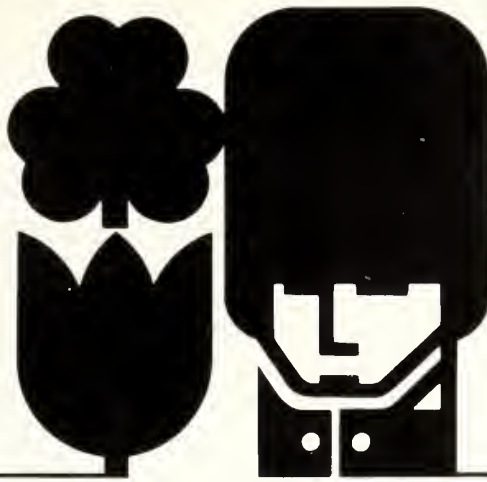
Directions for reconstitution

Reconstitute the lyophilized sodium levothyroxine by aseptically adding 5 ml of the Sodium Chloride Injection, U.S.P. to the vial. Shake vial to insure complete mixing. **Use immediately** after reconstitution. Discard any unused portion.

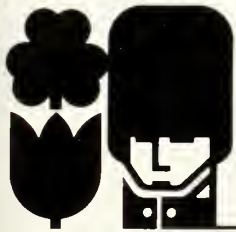


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 DIVISION OF TRAVENOL LABORATORIES, INC.
 Deerfield, Illinois 60015

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SOUTH CAROLINA MEDICAL ASSOCIATION



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Enclosed is my check for \$ _____ \$100 per person as deposit.

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Another Non-Regimented INTRAV Deluxe Adventure

A Method to Solve the Doctor Shortage

In the United States today, there is one doctor for every 650 people, or more doctors per capita than any other country in the world. Russia is next with one doctor per 750 people. However, as long as the Federal Government discriminates against the more equal distribution of doctors by discrimination against rural areas and small towns, we will never solve the maldistribution problem in the United States.

Not only do we see this discrimination on the federal level, we see it on the state level also. For example, South Carolina with a population of less than three million, less than greater Philadelphia, is divided into three economic areas as a basis for medicare and medicaid fee profiles: metropolitan, urban, and rural. These profiles are set up by the so-called customary and usual fees charged by the doctors in the designated areas the year prior to July 1st. Therefore, those doctors in the large cities, because of the higher prevailing fee schedule, rate higher fees for the same services than doctors can collect in the rural areas. As rural areas are often not as affluent as urban areas, rural doctors do not charge as much as urban doctors; hence, the system builds on itself.

No young doctor would move to a doctor-short community where he would be discriminated against economically. Why should he sacrifice cultural opportunities, time off, and the high fees of urban areas for the loneliness, long hours, and poor facilities of the rural. In fact, in my county in South Carolina with a population of 38,000, we recently had a young Cardiologist move from a metropolitan area, population 250,000, and medicare cut his fee profile thirty per cent. How can we expect doctors to move to the more rural area when this type discrimination not only exists but is encouraged by the government and backed by the AMA.

Country doctors have served the people in the rural areas with long hours, low fees and yet have earned little respect from their peers. The medical universities call them Local Medical Doctors. These doctors know their patients as friends and neighbors; they diagnose, treat, and cure them without the aid of expensive lab studies, consultants, and hospitals. Instead, they use compassion, knowledge, and common sense. And yet some newspapers say they are not needed, that paramedics can serve as well in the rural areas.

The State, the Federal Government, and yes, even the AMA, should begin to rewrite the laws to encourage a more equitable distribution of primary doctors (GP's, Internists, Surgeons, Ob-Gyn's, and Ped.) to those doctor-short areas. Some suggestions to encourage this more equitable distribution are: (1) a \$12,000 deduction allowed a doctor for federal tax purposes for ten years or for as long as his practice area is considered doctor-short, e.g., less than one primary doctor per 2,000 people; (2) government sponsored fees such as medicaid, medicare, and champus be the same for the same service all over the country. The Social Security taxes paid are the same; therefore, the first patient visit fee to the doctor would be the same in Gaffney, S. C., as in New York City. First hospital day, preparation of records, history and physical and institution of therapy would be the same for the doctor when paid by medicare in the small hospitals in rural Mississippi and in the large teaching centers in Chicago. The cholecystectomy would be worth as much for the medicaid patient in Alabama as in Los Angeles.

I believe that if the \$12,000 deduction and the equalization of government sponsored fees became a reality, you would see a more equitable distribution of doctors in the United States. It would then be

economically advantageous for him to move where he is needed. With such a system, I can foresee the day where every small community with a hospital would have adequate well-trained primary physicians, General Practitioners, Surgeons, Ob-Gyn's, Internists, and Pediatricians to serve them.

In my community, if we had one doctor for 1,500 people, we would have twenty-five doctors, or ten more than we have now. With ten additional doctors, our hospital would have no census problem, and the population would continue to have excellent medical care.

John H. Cathcart, M.D.

CLASSIFIED ADVERTISEMENTS

POSITION WANTED JULY 1975: 1974 MUSC graduate M.D., internship Richland Memorial Hospital, seeks position in north central SC. Write Placement Office, SCMA, P. O. Box 11188, Columbia SC 29211.

AUTOMOBILE: Mercedes Benz 1974, silver green, 450 SEL with sun roof, still on warranty, below cost, Columbia 787-2659.

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No investment, no paper work, excellent remuneration averaging \$52,000+ per year.

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SOUTH CAROLINA MEDICAL ASSOCIATION HOUSE OF DELEGATES

William H. Hunter, M.D., Speaker, Presiding
Forde A. McIver, M.D., Vice Speaker
J. Gavin Appleby, M.D., Parliamentarian

ORDER OF BUSINESS

Monday, May 5, 1975

9:30 a.m. Call to Order
 Invocation
 Report of Credentials Committee
 Opening Remarks by the President
 Introduction of President-Elect
 Announcement of Reference Committees
 Introduction of Special Guests
 Presentation of Resolutions and Recommendations

10:30 a.m. Report of Woman's Auxiliary
Reports of Officers:
The President, Donald G. Kilgore, Jr., to the membership of the South
Carolina Medical Association
The President-Elect, C. Tucker Weston
The Chairman of Council, Waitus O. Tanner
Reports of each District's Councilor have been included in the
House of Delegates Handbook and will not be read before the House.
Any supplementary remarks by the Councilors will be heard at this
time.
The Executive Director, Charles Johnson
The Secretary, D. Strother Pope
The Treasurer, J. Ernest Lathem
The Editor of the Journal, Edward E. Kimbrough
The Delegates to AMA

Reports of Committees:

Reports of the Committees will have been published in the **Journal** and in the House of Delegates Handbook and will not be read before the House. Any supplementary remarks by the Chairmen will be heard at this time.

Report of the State Board of Medical Examiners
Report of the State Board of Health and Environmental Control
Unfinished Business
 Amendments to the Constitution
New Business
 Announcement of new SCMA Logo

3:00 p.m. **Meeting of Reference Committees**
All members of the Association are invited to appear before the committees considering matters in which they are interested. Meeting places will be posted and announced.

Wednesday, May 7, 1975

9:30 a.m. Call to Order

William H. Hunter, M.D., Speaker

Report of Memorial Committee

Harold P. Hope, M.D.

Reports of Reference Committees

11:30 a.m. **Annual Elections**

Officers:

President-Elect

Vice President

Secretary

Treasurer

Delegate to the AMA (2-year term):

The term of Dr. John Hawk, Jr. (resigned to become Senior AMA Delegate) expires December 31, 1975. (The remainder of Dr. Hawk's term has been filled by Dr. Harrison Peeples.)

Alternate Delegate to the AMA (2-year term):

The term of Dr. C. Tucker Weston (resigned to become Senior AMA Alternate) expires December 31, 1975. (The remainder of Dr. Weston's term has been filled by Dr. W. L. Perry.)

Speaker of the House (2-year term):

The term of Dr. C. Tucker Weston (resigned to become SCMA President-Elect) expires. (The remainder of Dr. Weston's term has been filled by Dr. William H. Hunter.)

Vice Speaker of the House (2-year term):

The term of Dr. William H. Hunter (resigned to become Speaker) expires. (The remainder of Dr. Hunter's term has been filled by Dr. Forde A. McIver.)

Councilors (3-year term):

First District—The term of Dr. A. Richard Johnston expires (1969).

Fourth District—The term of Dr. J. Hal Jameson expires (1973).

Seventh District—The term of Dr. Michael Holmes expires (1966).

Mediation Committee (3-year term):

First District—The term of Dr. Arthur S. Jenkins expires (1972).

Fourth District—The term of Dr. William J. Bannen expires (1969).

Seventh District—The term of Dr. Davis D. Moise expires (1972).

Peer Review Committee (3-year term):

First District—The term of Dr. Thomas W. Messervy expires (1972).

Fourth District—The term of Dr. Lucius Cline expires (1972).

Seventh District—The term of Dr. Wallis D. Cone expires (1972).

Benevolence Fund Committee

The term of Dr. Lewis P. Jervey expires (resigned).

State Board of Medical Examiners (4-year term):

Second Congressional District—The term of Dr. Kirby Shealy expires.

Fifth Congressional District—The term of Dr. Roderick McDonald expires.

Selection of Place for 1978 Annual Meeting

Sine Die Adjournment

1:00 p.m. **Membership Meeting, South Carolina Medical Care Foundation**

SCIENTIFIC PROGRAM

May 6, 1975 Landmark Motor Inn



M. Gordon Howle, M.D.
Chairman, Scientific Program Committee

*Approved for 7 hours AAFP Credit and
AMA Physician's Recognition Award*

Dr. M. Gordon Howle has again brought together an outstanding group of speakers for SCMA's Annual Scientific Program. This year the program has been approved for AAFP and AMA Physician's Recognition Award credit. SCMA is proud to offer this fine program at the midpoint of the 1975 Annual Meeting.

8:30 a.m. - 9:30 a.m. Breakfast

—Grand Strand 1—

Dr. William Amols **Neurosurgery**

Dr. Walter M. Kirkendall **Internal Medicine**

—Grand Strand 2—

Dr. Theodore M. King **Ob-Gyn**

Dr. Andrew Whelton **Urology**

General Program

—Grand Strand 2—

10:00 a.m. Dr. Andrew Whelton
New Concepts in the Management of Urinary Tract Infections

11:00 a.m. Dr. William Amols
The Physiology of Muscle Tone

12:00 noon Dr. Theodore M. King
Venereal Disease—The Old and the New

12:40 p.m. - 1:10 p.m. Question and Answer Period

1:10 p.m. **ALUMNI LUNCHEON** Everyone Invited
—Main Dining Room—

2:30 p.m. Dr. Walter M. Kirkendall
A Personal Approach to the Diagnosis and Treatment of the Hypertensive Patient

3:30 p.m. Dr. William Amols
The Pharmacological Management of Abnormal Muscle Tone

4:10 p.m. - 4:30 p.m. Question and Answer Period

Scientific Speakers

William Amols, M.D. NEUROLOGY



Dr. Amols graduated from New York University College of Medicine in 1942 and his internship and residency in neurology at N.Y. City Hospital, Montefiore Hospital and Presbyterian Hospital.

He is presently Chief, Department of Neurology, Emazine Bassett Hospital, Cooperstown, N. Y., and Chairman, Department of Neurology, Cornell Medical School. He has published in such journals as JAMA, New England Journal of Medicine, N. Y. State Journal of Medicine, American Perfumer, and Headache, and is a member of numerous medical associations.

Andrew Whelton, M.B., B.Ch., B.A.O.

Dr. Whelton received his medical degrees in 1963 from the National University of Ireland. His internship and residency were completed at Johns Hopkins University School of Medicine. He had an extensive bibliography of his medical publishings. He presently holds the positions of Consultant in Renal Disease to the Surgeon General USAF; and Professor of Medicine, Johns Hopkins University School of Medicine; and Physician, Johns Hopkins Hospital.

Theodore M. King, Ph.D., M.D.
OBSTETRICS-GYNECOLOGY



In 1955, Dr. King was awarded his Ph.D. in Physiology from the University of Illinois School of Medicine. His residency in Ob-Gyn was completed at Sloane Hospital for Women, New

York City. He is a consultant to the N. Y. State Health Department, International Fertility Research Program, Sinai Hospital, National Women's Health Coalition, among others. He is now Professor and Director, Department of Gynecology and Obstetrics, Johns Hopkins University, Woman's Clinic 145, Baltimore.

Walter M. Kirkendall, M.D.
INTERNAL MEDICINE



Dr. Kirkendall received his M.D. from the University of Louisville College of Medicine in 1941. His postgraduate work was done in Iowa City and Louisville. He has published

more than 60 articles and is a member of numerous professional associations. Among his committee memberships are the USPHS Cooperative Study on Hypertension, International Society of Cardiology, and the Inter-Society Commission for Heart Disease Resources. He is presently Chairman and Professor, Department of Internal Medicine, University of Texas.

Rocky Mountain Spotted Fever Advisory

—By the S. C. Department of Health and
Environmental Control—

This is the time of year to increase the index of suspicion for Rocky Mountain Spotted Fever, also called tick typhus or American tick-borne spotted fever.

The South Carolina Department of Health and Environmental Control (DHEC) has observed a significant increase in the incidence of Rocky Mountain Spotted Fever in the state during the past 6 years. The first cases are usually reported in early May, with the peak number of cases coming in August.

Physicians are asked to be on the alert for febrile illnesses which follow tick bites or exposure in tick-infested areas. When Rocky Mountain Spotted Fever is suspected, serological confirmation is available from the Department of Health and Environmental Control Laboratory at 2600 Bull Street in Columbia. At least 2 serum specimens, collected 2 weeks apart, should be submitted to the State Laboratory in order to determine a rise in antibody titer. All cases should be reported to the DHEC Division of Epidemiology via the local county health department.

Severe headache, listlessness, myalgia, sudden chill, rapid rise in temperature and rash are characteristic symptoms of the disease and when a history of exposure to ticks is also present, the diagnosis is suggested. Symptoms may occur from two to twelve days after a person has been bitten by an infected tick. The distinctive rash usually appears on the extremities during the third day of the disease; early rash may resemble measles or other rash illnesses.

When diagnosed early, Rocky Mountain Spotted Fever can be treated successfully by the tetracycline drugs or chloramphenicol. Vaccines are available, but due to the questionable effectiveness of current vaccines and the low risk of contracting the

Rondomycin[®]

(methacycline HCl)

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines.

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.** **Usage in pregnancy.** (See above **WARNINGS** about use during tooth development.)

Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate observed in prematures given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Swelling of fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections, an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea. In uncomplicated gonorrhea, when penicillin is contraindicated, 'Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule: 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of 'Rondomycin' (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia: 900 mg daily for six days.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

SUPPLIED: 'Rondomycin' (methacycline HCl): 150 mg and 300 mg capsules; syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev. 6/73



WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512



**When the focus is on bronchitis due to
susceptible strains of *H. influenzae* and pneumococci***

Randomycin[®] 300 mg.
[methacycline HCl] Capsules

Delivers from the very first dose:

**studies show that after the first dose serum levels rapidly rise above
minimum *in vitro* inhibitory concentrations**

*Since many strains are known to be resistant, routine sensitivity testing is recommended

disease, the vaccine is recommended only for special situations such as laboratory personnel working with *Rickettsia rickettsii* and persons whose occupations result in repeated exposure to ticks in endemic areas.

Only live ticks that are removed from human beings should be mailed to the following address to determine if the tick is infected with a rickettsial organism.

Division of Vector Control
South Carolina Department of Health
and Environmental Control
2600 Bull Street
Columbia, South Carolina 29201

Due to the large volume of ticks submitted, we cannot examine those removed from animals or the environment.

It is requested that all live ticks submitted be placed in a medicine vial containing a small strip of paper towel moistened with *one drop* of water. Attached information should include date, locality, host, collector and telephone number of physician or patient. The sender can expect a telephone reply if tests are positive.

If a positive tick was removed from a patient whose signs and symptoms are compatible with a diagnosis of Rocky Mountain Spotted Fever, treatment can be initiated.

Fifty-five cases of Rocky Mountain Spotted Fever were reported in South Carolina during 1974, including five fatal cases. The fatalities were two young girls, ages two and five; a 49-year-old woman, and a couple in their forties. More than three-fourths of the cases reported occurred in the Piedmont or above the fall line.

The American dog tick, *Dermacentor variabilis*, is the most prevalent tick in South Carolina and a potential carrier of tick-borne typhus. Not all ticks are infected. Even in heavily-infested areas, only about one tick in twenty is infective and, therefore, able to transmit Rocky Mountain Spotted Fever.

PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

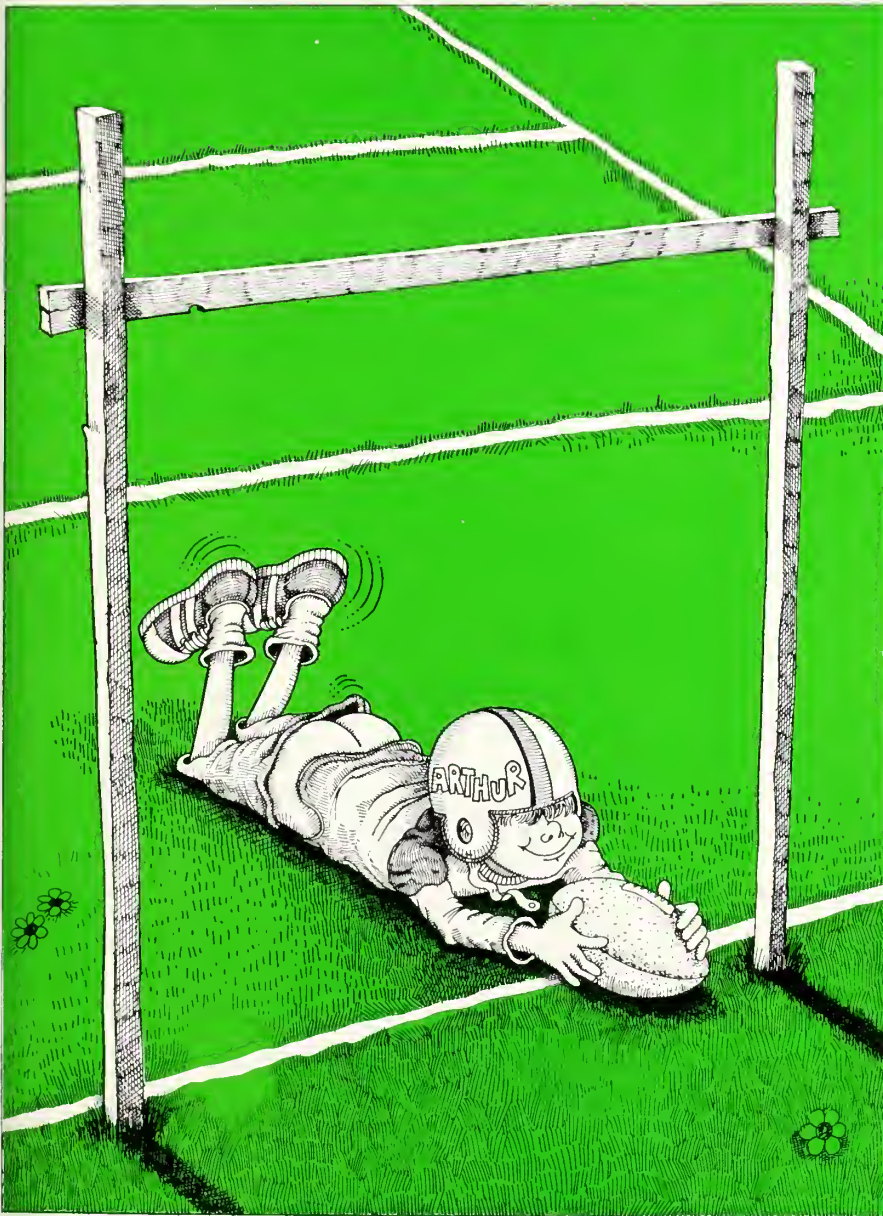
CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies*. Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

ROERIG **Pfizer**

A division of Pfizer Pharmaceuticals
New York, New York 10017

**Pinworms, roundworms controlled
with a single, non-staining dose of
ANTIMINTH[®]
(pyrantel pamoate)**

equivalent to 50 mg. pyrantel/ml.

ORAL SUSPENSION

*Data on file at Roerig.

Please see prescribing information on facing page

COMMITTEE REPORTS

(The report of the Maternal Health Committee appeared in the March issue of *The Journal*, pp. 77-82; additional reports will appear in the House of Delegates Handbook)

Committee on Mental Health

- I. The Committee on Mental Health was charged with the responsibility of investigating and reporting on the forced resignation of Roy Suber, M.D., as superintendent of Whitten Village. The investigation was carried out and a meeting was held with representatives from the State Commission on Mental Retardation. However, these representatives refused to turn over to the Committee its prepared statement which they brought to the meeting. A long discussion was held and the Committee was assured that Dr. Suber was not forced to resign because of anything relating to his moral or professional conduct. It was said to be an administrative matter. It was the opinion of the Committee that no adequate cause for his dismissal was found and the Committee prepared and submitted a resolution commending Dr. Suber for his years of service to the mentally retarded of South Carolina. This was adopted at the mid-winter meeting of the House of Delegates.
- II. The Committee emphasized the need for increased input and participation in the very earliest stages of mental health planning and legislation pertaining to mental health and mental illness in South Carolina. SCMA should actively strive to have representation at every meeting of the Joint Legislative Committee on Mental Health and Mental Retardation and strive to get physician representation appointed to this Committee.

- III. The Committee has been working to obtain amendments to the 1974 law pertaining to admission to and discharge from mental hospitals. It is unlikely that the adversary type hearing acquired by this law can be significantly modified because the federal courts have held that this is a requirement in order to protect the rights of the mentally ill. Some of the recommended changes are as follows:
 1. The thrust of the law is almost entirely toward the rights of the mentally ill but, in attempting to protect their rights, in certain instances the law severely jeopardizes their welfare. Patients have been transported back to the county of origin for the required examinations. Some provision needs to be made for the severely physically ill patient where transportation would be hazardous to his health and also for the severely disturbed mentally ill patients who cannot be transported without unreasonable danger to themselves or others. The only places these examinations can safely be done are at the state hospitals. It should be emphasized that during the period in which new patients are undergoing the examinations and hearing their treatment programs are being interrupted and the net result will be a longer stay in the hospital because of these proceedings.
 2. The consensus of the Committee was that the hearings and examinations should be held at the State Hospitals. If this cannot be accomplished, the examinations and hearings should be channeled through the area mental health centers with the hearings being conducted at the mental health centers. It was felt that the mental health centers could coordinate a program for the county or counties that they

serve and either hire individuals or contract with physicians or designated examiners to do the examinations and the process could be made to work much more efficiently. The law may have to be changed to give the probate judges authority to hold hearings of this type outside of their own county.

3. Some provision needed to be made in the law for temporary detention in an emergency of people who are mentally ill in a holding room or seclusion room of hospitals while the legal requirements of the law are being carried out.

4. Under Section 32-994, electric

shock treatment is placed in the same category as lobotomy and in South Carolina electric shock treatment is considered a standard psychiatric treatment and such severe restrictions regarding its use should not be legislated.

5. The compensation for physicians for the examinations and hearings should be raised to \$50.00 per hour.

6. Provision should be made for payment for a conference with the family or other interested party by the designated examiners.

Respectfully submitted,

R. Bruce Ford, M.D.

Chairman

Insurance Committee

This S.C.M.A. Insurance Committee report will be the last one I will be making to you. After six years filled with fast moving developments in the insurance related field, I think the time has come for me to pass this committee chairmanship to another energetic member.

During the past year we have been reviewing all our insurance programs. Some changes will be made but most programs will remain basically the same. One change was the switching of the accidental disability insurance from American Home Insurance Co. to Reliance Insurance Co. through the Sadler Insurance Agency. We had to do this to keep the provisions and the premiums the same.

We conducted a survey in February,

1975, in regards to our Blue Cross-Blue Shield group insurance program. The survey revealed very little support for a low level benefit program and therefore none will be offered.

The majority supported the current program and it will be maintained. A considerable minority expressed support for the current program plus outpatient diagnostic and psychiatric riders; therefore, we will offer this as an option. Our current health program expresses the will of the members as revealed in the survey and we hope those who are dissatisfied will appreciate the will of most of our members.

Harry J. Metropol, M.D.

Chairman



FINANCIAL CORNER



STOCK OF THE MONTH

Xonics—Xonics, formed in 1970, is a high technology company specializing in medical diagnostic equipment. The company has developed a new technique for X-raying called electron radiography (ERG). This technique uses the same basic equipment as conventional methods. Instead of using the normal silver halide X-ray film, however, an electrostatic image is produced on a thin plastic (mylar) sheet. Among the advantages of ERG are quicker development, lower radiation exposure, better image resolution, lower costs and convenience. In 1973, a 15-year \$5.3 million agreement was consummated with Agfa-Gevaert, Europe's largest producer of X-ray equipment, for the dis-

tribution of ERG products in Europe, Africa and South America. Aside from its medical products, Xonics is active in environmental monitoring systems, radar equipment and Telepost, a service which allows customers access to the Western Union/U.S. Postal Service Mailgram. More than half of total revenues comes from Government contracts. Through the initial three quarters of the current fiscal year ending March 31, per share earnings dipped to \$0.22 from \$0.24 for the similar interim the year before. While these shares are extremely aggressive, they do offer interesting long term potential for accounts willing to assume significant speculative risk.

JSCMA Portfolio of Dow Recommended Stocks

Stock	Date	Purchase Price	Present Value	Dividends (added yearly)
RCA	1 Feb 75	\$1100	\$1565	\$1.00/share
Xonics	18 Mar 75	100x\$16.50=\$1650	\$1650	none



NEW SITE FOR SOUTH CAROLINA MEDICAL ASSOCIATION

As of February 3, 1975, the South Carolina Medical Association has occupied its permanent home at 3325 Medical Park Road in Columbia.

The new building is bounded on the east by Richland Memorial Hospital, and on the west by Bull Street Extension.

Headquartered in the building along with the Association are the South Carolina Medical Care Foundation and PSRO, and the Columbia Medical Society.

the weight of scientific opinion:

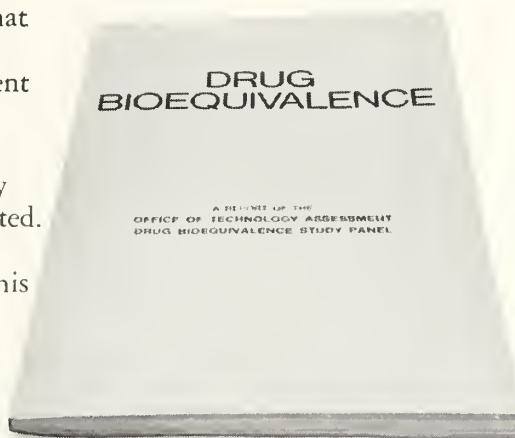
If the pharmacist substituted a chemically equivalent drug for the one you have specified for your patient—could you be certain of that product's safety and effectiveness simply because the chemical content was the same?

Definitely not, unless bioequivalence tests and other quality assurance checks had been conducted. The pharmaceutical industry and many scientists have maintained this position for years, but others have questioned it. Now the Office of Technology Assessment of the Congress of the United States has reported on the issue in its Drug Bioequivalence Study.*

Here are a few definitive statements in the O.T.A. report:

"...the problem of bioequivalency in chemically equivalent products is a real one. Since the studies in which lack of bioequivalence was demonstrated involved marketed products that met current compendial standards, these documented instances constitute unequivocal evidence that neither the present standards for testing the finished product nor the specifications for materials, manufacturing process, and controls are adequate to ensure

that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.



"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and

(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or (c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...



Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

protecting the integrity of your prescription

INAUGURAL ADDRESS

CHARLESTON COUNTY MEDICAL SOCIETY

Leon Banov, Jr., M. D.
December 10, 1974

At the outset I want to express not only my heartfelt but my deep seated appreciation for the honor to serve as president of the Charleston County Medical Society as we enter the last quarter of the twentieth century. I am especially touched because you have selected as the leader one who is always behind in his work. As Ken Boniface has said, I am the only person he knows who gets ahead by being behind in his work.

I want to commend Louis Jervey for his impressive and effective leadership carried out with dignity and conscience during the past two years. I have learned a lot. I hope I can do half as well as he did.

I look forward to working with Biemann Othersen, the effective and dependable secretary-treasurer.

Included in the leadership is the president-elect, Bill Cain, ready, willing and able to receive the gavel two years from now.

I am mindful that this society is also indebted to the effective leadership of other past presidents who have devoted their time and talent to guide this society.

After following all these illustrious leaders, I have mulled over what unique attributes I bring to this presidency.

I have attended and have participated in my share of regional, national and international meetings. So have the other past presidents. But, since I treat only anorectal diseases, you must have regarded that as an asset.

I do cultivate the hobby of avidly studying medical history. History is not likely to come up with specific answers to questions of practical policy, but it does provide a long range view, so helpful in working towards solutions for human

problems. Yes, knowledge of the past is nice but what of the present?

For the past year and a half I have been privileged to serve on H.E.W.'s Food and Drug Administration Advisory Panel on OTC Hemorrhoidal Drugs. Meeting every six or eight weeks on weekends in Washington I have learned a great deal about how governmental bureaus function. As you know, we are governed not only by legislation passed by Congress but even more so by regulations from the various executive departments through the Public Register. One of the first lessons I learned was that well-researched, clearly-stated, accurately-documented reports possess much more clout than do emotionally charged shrieks.

With this background I pledge to you to do my best to serve during the next two years.

Since ours is an age of crisis and social upheaval, a transitional period marked by revaluation of all values, we can look forward to two exciting years.

And now I address you as my fellow Esculapians, Disciples of Esculapius. As I assume the presidency I think it beneficial now to pause and to reflect on the purpose of this Charleston County Medical Society. Turning to the Constitution, the stated purpose is to "organize the physicians of Charleston County for scientific and professional purposes." Everyone understands the meaning of "scientific purposes." However, I have a feeling that many are unable to define what is meant by "professional," nor do they know the history of the development of the medical profession. Just what is meant by "professional purposes" is not stated in the Constitution nor in the by-laws! Before we can carry out our professional pur-

poses, we should develop an understanding of what is meant by the term "professional." How did the medical profession come into being? What is meant by a professional organization? What is expected of a professional organization?

Vern Bullough wrote that "a profession is a high prestige occupational group, with considerable power over self regulation, and a special style of life. It is not necessarily altruistic, although its aims are sometimes put in altruistic terms, but its chief motivating factor is enlightened self interest which can also be justified for the sake of public welfare." In simple terms a profession is a high status group which has become institutionalized.

Professionalization is now a part of our culture. It can be looked upon as beneficial to society—encouraging educational expectations. Modern professions have become so much a part of our society it is hard to imagine how we can get along without professions. Studying and working to be identified as a professional is one of the motivating factors in our culture. In previous years people wanted a white collar job to achieve respectability. Now people aspire to become a professional. A person who sells real estate wants to be identified as a realtor, which denotes a professional standing.

Looking back to the past, in the medieval period medicine emerged as a profession to take its place along side the liberal arts, law, and theology as part of the curriculum of the university. This is the major contribution of medieval medicine to modern medicine and one that still affects its practice and its outlook. Medicine, one of the first professions to emerge, has attained a high status and has been imitated by other groups. In effect, the medical profession has come to be regarded as the pace-setter. It now falls upon this generation to continue and to advance the medical profession. In this Charleston County Medical Society we now have that opportunity.

A decisive factor in the emergence of

medicine as a profession was the development of a body of knowledge that was unknown to the average layman. Previous medical knowledge was a part of the general information of most well educated people. In the later medieval period, with the rising importance of universities, medical knowledge became institutionalized and available to those who did graduate work. The standards for graduation were set by the medical practitioners themselves. Then, as now, there were groups competing for the delivery of health care. To distinguish themselves from others who practiced the healing arts, the physicians established qualifying associations—hence the creation of professional organizations.

This points out the need for bringing about a better relationship between those who teach medicine and those who practice medicine. One of the chief goals in the training of medical students is to initiate them into a set of professional attitudes and controls, to give that person a professional conscience and to develop a feeling of group solidarity. The medical school doesn't make doctors; it simply gives interested students the intellectual tools to become doctors.

The medical school should not only teach the history of scientific advances but should also include the history of the development of medicine as a profession. In celebrating its sesquicentennial, the Medical University of South Carolina has called attention to its creation, maintenance, and development brought about by the private practitioners "in town." It would seem a desirable goal for this Charleston County Medical Society to promote a closer more harmonious working relationship between the so-called gown and town. On many occasions, the late Dr. Colbert emphasized to me, "We are all in the same boat." Hence, the Charleston County Medical Society provides the organization for both gown and town to work harmoniously and effectively for the good of society and for the betterment of

the medical profession. A better relationship between both can be achieved if those in gown get to know better those in town, and vice versa. The Charleston County Medical Society is the only organization that promotes the professional interests of both.

Medieval physicians, regardless of their professional image were seldom shy about charging high fees. Henri de Mondeville (1260-1320) stated that three facts should be taken into consideration for setting fees: the standing of the physician in the profession, the condition of the patient, and the seriousness of the illness. Today, the trend of society is to try to set one fee for each type of service. (Need I say more about the urgency to promote professional solidarity?)

Basically, it is in the self-interest of physicians and surgeons to adhere to as high a code of ethics as possible. Such adherence is a necessity. A profession must have some sort of ethics, the rules of the game which each practitioner attempts to follow. Self regulation is necessary to justify exclusionary tactics, to set fees, to regulate other medical practitioners, or whatever else needs justifying. Our ethics are neither so altruistic as some advocates of professionalization have believed, nor quite as base as some of the critics of medicine have alleged.

We have inherited all the benefits of a great profession—a profession that has supplied us, is supplying us and, we hope, will continue to provide us with the many good things in life. Each individual is personally benefitting or has the potential to benefit because he is in the medical profession. Stated as an overview, the individual

practitioner of medicine is getting rich while the professional body, the organization or the source of the individual's power, is getting relatively poorer. Never should we forget that we have what we have because in the historic past many have worked zealously for the cause of the medical profession. We have an unrepaid debt to the previous generations of physicians who promoted the profession of medicine in Charleston.

Sir William Osler said the first and most important function of a (local) medical society was "to lay a foundation for that unity and friendship which is essential to the dignity and usefulness of the profession. Unity and Friendship! How we all long for them, but how difficult to attain!"

It is obvious that unless the profession is better organized and has more unity the individual practitioner will suffer. This organization which has promoted the profession in the past needs your support now to make it strong enough to work effectively for you in the years ahead.

I earnestly urge you to join together to give affirmative action now to promoting the professional purposes of the Charleston County Medical Society.

And so the gavel of the presidency is passed on to me hopefully not in sorrow but with the hope of building a better tomorrow. We have the continuing opportunity, you and I, to prepare for the future. Our preparations are made with a great deal of hope. It is this Preparation Hope that will ever encourage us to achieve the goals for the medical profession in the Charleston area.

**KENNETH MERRILL LYNCH, M.D.,
D.Sc., LL.D.**

Kenneth Merrill Lynch was born in Hamilton County, Texas, on November 27, 1887, and died November 29, 1974. After receiving his M.D. degree from the University of Texas in 1910, he took his graduate training in Philadelphia, becoming instructor in Pathology at the University of Pennsylvania and assistant pathologist of the Philadelphia General Hospital and University of Pennsylvania Hospital.

His association with the Medical College of South Carolina started in 1913 when he arrived to serve as Professor of Pathology and first full time member of the faculty. He served as Vice Dean of the Medical College from 1935-43; as Dean from 1943-49; and as President and Dean of the Faculty from 1949-60. In the latter year he was appointed Professor Emeritus of Pathology and Chancellor.

He published some 118 papers in medical science and educational periodicals. Dr. Lynch was one of the first to recognize the occurrence of granuloma inguinale in this country and played a major role in its control. He was a pioneer investigator of industrial diseases of the chest, particularly asbestosis. He published the first full description of kaolinoses and reported the first recorded case of cancer of the lung associated with asbestosis.

In 1934 he was selected American editor of Green's Manual of Pathology, published both in England and America. In addition he served on the editorial boards of the American Journal of Tropical Medicine, the American Journal of Clinical Pathology and the Journal of Digestive Diseases and Nutrition.

Dr. Lynch was quite active in the South

Carolina Medical Association, serving as President in 1930-31. He was honored with numerous executive appointments in the Southern Medical Association; as Vice President of the American Medical Association, presiding at the convention of 1936; on the Board of Governors of the American College of Physicians; as President of the American Society of Tropical Medicine and of the American Society of Clinical Pathologists.

Dr. Lynch won the gold medal of the American Medical Association in 1921 for his scientific exhibit on Granuloma Inguinale and the Research Medal of the Southern Medical Association that year, the Distinguished Service Award of the Southern Medical Association in 1957; the Distinguished Service Citation and Medal of the American Cancer Society in 1958; and the Ashbel Smith Medallion and Award for Distinguished Service to Medicine from the University of Texas in 1967.

He also received honorary degrees from the University of South Carolina, the College of Charleston, and Clemson University.

Dr. Lynch wrote or co-authored six books, two of them dealing with the history of the Medical University—*Medical Schooling in South Carolina* and the Sesquicentennial Commemorative Volume.

In 1944 Dr. Lynch became head of the Medical College and served notably in the development of the Medical University, his programs and accomplishments advancing the institution in its medical educational research and service commitments to such a degree as to fulfill the modern concept of a medical center.

The Upper Functional G.I. Disorder

The Pseudo-ulcer

Ulcer-like symptoms: no G.I. pathology



X-ray demonstrates normal stomach.

The patient is convinced he has an ulcer. However, symptoms are not quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient understand how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist.* Where milder cases may respond to counseling alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms.

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*Rome HP, Brannick TL: Orientation and mechanism of functional disorders; clinicophysiology correlation, chap. 133, in *Gastroenterology*, edited by Bockus HL. Philadelphia, W.B. Saunders Company, 1965, p. 1116.

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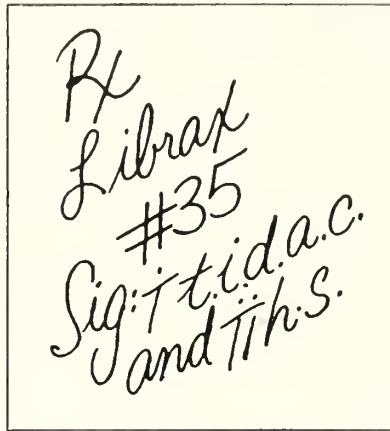


Please see summary of product information on following page.

upper functional G.I. disorders

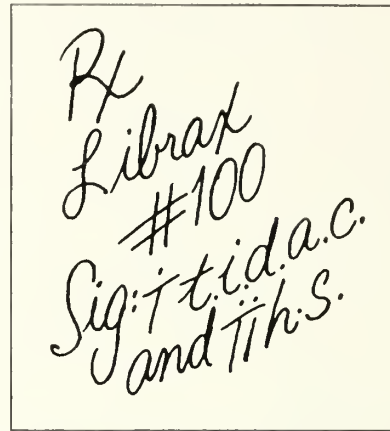
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The initial prescription allows evaluation of patient response to therapy.



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Follow-up therapy with a prescription for 2 to 3 weeks' medication usually helps maintain patient gains.

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Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures

necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

Dosage: Individualize for maximum beneficial effects. Usual maintenance dose is 1 or 2 capsules, 3 or 4 times a day, before meals and at bedtime. Geriatric patients—see Precautions.

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MEMOIRS OF WILLIAM A. BOYD, M. D.*

JAMES T. GREEN, M. D.

Mr. President, members of the South Carolina Orthopaedic Association, ladies, and special guests, Dr. and Mrs. Enneking:

I feel greatly honored and pleased to have been asked to be the first to present the Billy Boyd Award. This is an award for excellence in ability to diagnose the tricky films and histories as presented each year.

I was asked to give you a little background on the life and personality of Dr. Boyd. It seems to me that everybody in this organization should personally have known him; however, the other day when I spoke to our secretary, Dr. Hay, on the 'phone, he said that he had never met Dr. Boyd.

Dr. Boyd was, of course, the organizer of the South Carolina Orthopaedic Association, and it would seem that he has always been present at its meetings. I knew Dr. Boyd well. He was one of a kind and represented an era in the practice of medicine in South Carolina, which ended at the time of his death in 1961. He was interested in the patient's welfare—totally, medically, economically, sociologically. He was not in favor of the supermarket type of practice of medicine, and maintained his family practice attitude until the end. He has often related how he had walked to West Columbia to see a patient for a fifty cents fee or for farm produce.

Dr. Boyd was born in Charleston U.S.A. His family was a distinguished family who moved from Ireland to Charleston just after the War Between the States. His father had a plantation named Bay-

view which was just outside of Charleston. Incidentally, they grew the first asparagus in the U. S. A. He had his early education in Charleston, going to high school and then to the College of Charleston. He received his M. D. degree from the University of Pennsylvania School of Medicine in 1903. Prior to this, however, in 1899, he received a diploma from the Philadelphia School of Anatomy, and this training he always valued very highly. Dr. Boyd interned at the Howard Hospital in Philadelphia and, at the same time, he was chief resident in the Philadelphia Orthopaedic Hospital. We can see from this that moonlighting has been going on for many years—Dr. Boyd may have started it. At the Orthopaedic Hospital, he laid the foundation for his future career.

Dr. Boyd originally started practice as a general practitioner in Columbia in 1904. He served as health officer in Columbia from 1910 to 1915. He had to deal with smallpox epidemics. His stories regarding the handling of the serious epidemics were amazing. In 1918 he limited his practice to Orthopaedic Surgery. He started an orthopaedic clinic in Columbia, and had great trouble getting funds for the crippled children's work that he was doing. He requested, and received, favorable action from the South Carolina General Assembly for \$5,000.00 in 1923. This clinic eventually led to the State Crippled Children's Clinics, and these remained dear to his heart his whole life.

He married Miss Mary Keller and they had one daughter, Mary Keller Boyd.

Dr. Boyd served as a consultant to the draft board during the first World War and was a member of the volunteer medical service corps. In the second World

*This paper was presented at the South Carolina Orthopedic Association meeting in September 1975 in honor of South Carolina's first and one of our most eminent orthopedists by a slightly younger but no less eminent orthopedist.

War, he was a member of the Medical Advisory Board to the Selective Service.

Dr. Boyd was very active in medical organization in South Carolina, as well as in the United States. He was President of the South Carolina Orthopaedic Association for a period of ten years. In 1960, he was presented a plaque by this Association, honoring him for the guidance he had given to the Association, and for his pioneer work in the field of Orthopaedic Surgery. He was Vice President of the South Carolina Medical Association, President of the Columbia Medical Society, Chairman of the Advisory Board of the South Carolina State Board of Health. He was a member of the Southern Surgical Association, a member of the American Orthopaedic Association, American Academy of Orthopaedic Surgeons, the Georgia and North Carolina Orthopaedic Associations, American College of Surgeons, Southeastern Surgical Association, American Association of Railway Surgeons, and many others. He was President of the Medical Society of three railways, namely, the Southern, the Seaboard Air Line, and the Atlantic Coast Line. This has not been held by any other. He was an honorary member of the Blue Key Society of the University of South Carolina. He was a Kiwanian.

As you see from what I have just related, Dr. Billy was an outstanding man from the standpoint of his curriculum vitae. In addition to these attainments, he was an outstanding conversationalist and raconteur. He had a personal charm that was marvelous. His manner was Chesterfieldian and would have probably outclassed Lord Chesterfield. He was an impeccable dresser. I am not sure that he would be in favor of lace on the cuffs; however, I am sure he would not favor lace on the shorts. He wore hand-tailored suits and he always wore a red rose in his lapel. He loved to dress for dinner. On such an occasion as this, he took great pride in so honoring the President of the Organization by his dress. He was a de-

light at any social gathering, and was particularly pleasing at cocktail parties. It was not difficult to get him to agree to a hurriedly called party or to participate in a libation. He felt that flowers were essential to a party and, not infrequently, he would suggest that I have a party and he would bring the flowers. He had the ability to use many dialects and was great with pantomime. With his ability to speak and to relate stories, and to act out many of his stories, he thrilled thousands in his audience. He loved to hunt, and many of his stories were related to this.

One of the stories that I recall so well from Dr. Boyd was one that he told on many occasions and related to his early experience in Columbia. Shortly after starting to practice, he was giving an anesthetic for Dr. Julius Taylor, who was going to do a mastoidectomy on a big male negro. Dr. Boyd would tell in great detail how the tin instruments of that day were soaked in a little bichloride of mercury solution, and the surgeons would likewise dip their hands in the bichloride solution for cleansing and sterilization. Dr. Boyd told how he made a cornucopia and started pouring chloroform. After a little bit, the patient started to doze and then progressed to a very deep, loud snore. Dr. Boyd then, assured that the patient was asleep, stepped back, and in his Chesterfieldian manner, bowed low, and told Dr. Taylor that his patient was ready. Dr. Taylor took a little bichloride solution, pulled the ear forward and wiped over the mastoid, then took his tin knife and made a little incision. He took his chisel and mallet and started to open the mastoid. After he had struck the mallet a few times, the big negro suddenly raised to a sitting position, looked around, and said "who dat knock?" The way that Dr. Boyd could tell stories such as these was like unto no other that I have ever heard. He always had a good story to tell, and it was of a variety that could be told in any company.

On one occasion, Dr. Boyd, Dr. Theo-

dore Hopkins, Dr. Charles Epting and I, were on the dining car of a train going to a medical meeting. Dr. Hopkins, after a few drinks, told Dr. Boyd that he knew Dr. Boyd was getting old and wanted him to know that everyone loved him; that when Dr. Boyd died, Dr. Hopkins would give Dr. Boyd one of the finest funerals anybody had ever had. It would be at Trinity Church, there would be lots of flowers, all of the Columbia Hospital nurses would be on one side of the church, and all of the doctors would be on the other side. It would be a grand funeral. Dr. Hopkins promised Dr. Boyd that he would stay at the grave side after the

funeral when the grave was closed, and that he would not allow any clods to be thrown on his face. Dr. Boyd listened to the plan for his funeral and enjoyed it tremendously, and kidded Dr. Hopkins about it for many years.

I tried my best to have him record some of his stories for posterity, but he never got around to it.

It is with a great deal of pleasure that I present the new Revere Bowl as the Dr. Billy Boyd Award to its first official winner for his outstanding diagnostic ability, Dr. Dayton Riddle of Greenville, South Carolina.

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OF THE COLLEGE OF MEDICINE**

- May 2-3 Pediatrics—Robert W. Winters, M.D., of Columbia University, and Albert B. Sabin, M.D., of the Medical University of South Carolina, Visiting Speakers. This seminar will be held in conjunction with the meeting of the South Carolina Pediatric Society and the South Carolina Chapter of the American Academy of Pediatrics.
- May 16-17 Thoracic Surgery — Denton A. Cooley, M.D., Surgeon-in-Chief of the Texas Heart Institute, Houston; W. Leigh Thompson, Jr., M.D., Ph.D., of Case Western Reserve University; Priv. Dr. K. Messmer of Universitäts-Klinik, Munich, Germany; Karl E. Arfors, M.D., of Pharmacia, Upsala, Sweden; and George A. Clowes, Jr., M.D., of Harvard University, Visiting Speakers.

Please notify the appropriate department if you expect to attend. Medical University of South Carolina, 80 Barre St., Charleston, S. C. 29401.

**PERSPECTIVES IN MEDICINE — MAY 9-10, 1975
PROGRAM**

Friday Afternoon, May 9, 1975, 2:30 P.M.

Lewis Thomas, M.D., President of the Memorial Sloan-Kettering Cancer Center, will speak on "Science and the Future of Medicine."

Albert B. Sabin, M.D., Distinguished Research Professor of Biomedicine, Medical University of South Carolina, will speak on "Perspectives in Biomedical Research."

Saturday Morning, May 10, 1975, 10:30 A.M.

H. Rocke Robertson, M.D., former President of McGill University and Distinguished Surgeon of Ottawa, Canada, will speak on "What One Can Expect in Changes in Health Care in the Next Twenty Years."

Malcolm C. Todd, M.D., President of the American Medical Association, will speak on "The Future of Health Care in the United States."

The sessions will be held in the Auditorium of the Basic Science-College of Dental Medicine Building.



WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION

Call To Convention

Registration

Coffee Shop Area, Landmark Motor Inn

Sunday, May 4 -----3:00- 5:00 P.M.

Monday, May 5 -----8:30-11:30 A.M.

Tuesday, May 6 -----8:30- 9:30 A.M.

52nd Annual Convention

Landmark Motor Inn

1501 South Ocean Boulevard

Myrtle Beach, South Carolina

May 4, 5, 6, 7, 1975

Sunday, May 4, 1975

4:00 P.M. Finance Committee Meeting, President's Suite #526, Landmark

Monday, May 5, 1975

8:30-9:30 A.M. Complimentary Continental Breakfast, Coquina Room, 4th Floor, Landmark

10:00 A.M. Executive Board Meeting, Coquina Room, 4th Floor, Landmark
Mrs. Wayne C. Brady, President, presiding.

1:30 P.M. Luncheon with Husbands, Grand Strand Ball Room, 4th Floor, Landmark

Guest Speaker: Governor James B. Edwards

3:00 P.M. Round Table Conference, Coquina Room, 4th Floor, Landmark

7:00 P.M. Auxiliary Social Hour, Grand Strand Ball Room, 4th Floor, Landmark

8:00 P.M. Buffet Dinner and Entertainment by Miss South Carolina

Tuesday, May 6, 1975

8:30-9:30 A.M. Complimentary Breakfast, Coquina Room, 4th Floor, Landmark

10:00 A.M. House of Delegates Meeting, Colonial Room, Pine Lakes International Country Club

Mrs. Wayne C. Brady, President, presiding.

1:00 P.M. Membership Luncheon, Pine Lakes International Country Club

Guest Speaker: Mrs. Norman Gardner, 1st Vice President, AMA Auxiliary

Honored Guests: Past State Presidents of Auxiliary

2:30 P.M. Post-Convention Board Meeting, Colonial Room, Pine Lakes International Country Club

Mrs. Wayne C. Brady, presiding.

7:00 P.M. SCMA Reception and Banquet, Grand Strand Ball Room, 4th Floor, Landmark

Donald C. Kilgore, M.D., President, South Carolina Medical Association, presiding.

Guest Speaker: Neal Pierce, Author, Lecturer, & Political Commentator

PRE-REGISTRATION FORM
FOR CONVENTION
WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION
May 4-7, 1975

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Check Desired Activity and Include Check, Payable to Woman's Auxiliary to SCMA

Sunday, May 4, 1975

Registration 8:30-11:30 A.M., Coffee Shop Area, Landmark Motor Inn

Monday, May 5, 1975

Registration 8:30-11:30 A.M., Coffee Shop Area

- () 8:30-9:30 A.M. Complimentary Continental Breakfast, Coquina Room, 4th Floor, Landmark

- () 10:00 A.M. Executive Board Meeting, Coquina Room, 4th Floor, Landmark
- () 1:30 P.M. Luncheon with Husbands, Grand Ball Room, 4th Floor, Landmark
Special Guests: Gov. and Mrs. James Edwards
Price per person: \$5.25

- () 7:00 P.M. Auxiliary Social Hour, followed by Buffet Dinner, 8:00 P.M.
Grand Strand Ball Room, Landmark Motor Inn. Fabulous entertainment by Miss South Carolina, Cheryl von Lehe.
Husbands cordially invited. Price \$12.00 per person.

Tuesday, May 6, 1975

Registration 8:30-10:00 A.M., Coffee Shop Area, Landmark Motor Inn

- () 8:30-9:30 A.M. Complimentary Continental Breakfast, Coquina Room, 4th Floor
- 10:00 A.M. General Meeting, House of Delegates, Colonial Room, Pine Lakes International Country Club

- () 1:00 P.M. Membership Luncheon, Past State Presidents Honored. Pine Lakes International Country Club, Mrs. Norman Gardner, 1st Vice President, AMA Auxiliary, Speaker
Price \$6.00 per person

- 2:30 P.M. Post-Convention Board Meeting, Colonial Room, Pine Lakes Country Club

- () 7:00 P.M. SCMA RECEPTION AND BANQUET, Grand Ball Room, 4th Floor, Landmark. Remind your husbands to secure these tickets through SCMA

REGISTRATION FEE FOR EACH MEMBER — \$1.00

Reservation forms with check, should be mailed prior to April 25, 1975, Mrs. Laurie N. Ervin, 44 Stillwood Drive, Greenville, S. C. 29607. Tickets will be held at pre-registration desk in Coffee Shop Area of Landmark Motor Inn during registration hours ONLY.

NOTE: Pre-registration for the various activities, with your check, must be made by April 25, 1975 DEADLINE. No tickets available at convention.

This is necessary to help make YOUR CONVENTION a success. Thank you!



Mrs. Wayne C. Brady

I would like to take this opportunity to pay tribute to the South Carolina Medical Association. To Dr. Kilgore, president, my sincere thanks for always being available to my Saturday and Sunday afternoon phone calls. Being neighbors on the same street, I'm sure he didn't count on having his weekend at home interrupted with Auxiliary business. To Dr. Waitus Tanner, Chairman of Council, my gratitude for his understanding in examining objectively the request made by the Auxiliary this year that will greatly benefit the working relations of the Auxiliary and the Association. To the Advisory Council for the Auxiliary, thanks so much for always being there, and especially to my husband, who is a member of the Advisory Council, my special thanks for letting me interrupt his reading or a ball game to ask his opinion, tie up the telephone, work hours into the night on the typewriter, and not always have his dinner on the table. To Mr. Johnson, it has meant so much to the Auxiliary and to me this year to have your help, support and advice.

The members of the Auxiliary have

tried to be a credit to the Association. I have traveled over thirty-three hundred miles throughout the state this year and have seen the county auxiliaries in action. We are involved in Child Protection Forums and programs, and many of our members serve on county multi-disciplinary committees. There has been eye-screening in the public schools, volunteers working with hypertension screening, pap smear clinics and cancer educational programs. The Auxiliary is concerned about the aging and has been active in home-bound programs and assisted with meals-on-wheels programs. The patients in the State Hospital have also been remembered.

The communities throughout our state are feeling the impact of the work of the Medical Auxiliary. The image of the doctor's wife has changed, and is changing. We are no longer being thought of as the bridge club society crowd, but women interested in our husband's profession, caring and doing something about the health and needs of the people of our communities and state.

We care about the future of medicine also and are working with Health Career Clubs in the schools to promote interest in all health fields. Last October the Auxiliary sponsored a health careers rally in Charleston that attracted 3000 high school students. We have been busy raising money for AMA-ERF for our medical schools and student loan fund.

We appreciate the privilege of having a page in the Journal of the South Carolina Medical Association each month. It has proven to be a source of communication to the Association as well as the Auxiliary.

I sincerely hope that through communication, the members of the Association will become more aware of the purpose and work of the Auxiliary, and will encourage the wives that are not members to come and join us.

Billie Brady
President, SCMA Auxiliary

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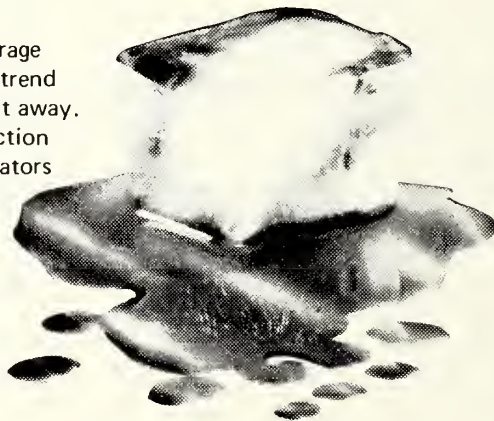
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A high assurance of clinical efficacy

- in cystitis, pyelonephritis and pyelitis diagnosed as chronic
- against susceptible strains of the common urinary tract pathogens, usually *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, and, less frequently, indole-positive proteus species.



Before prescribing, please consult complete product information, a summary of which follows:

Indications: Chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, and, less frequently, indole-positive proteus species).

Note: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in chronic and recurrent urinary tract infections.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, granulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia in elderly patients on diuretics, primarily thiazides. Sore throat, fever, pallor or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. Data are insufficient to recommend use in infants and children under 12.

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, allergy or bronchial asthma; and in those with glucose-6-phosphate dehydrogenase deficiency, where hemolysis may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus,

exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12.

Usual adult dosage: Two tablets b.i.d. for 10 to 14 days. For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	2 tablets every 24 hours
Below 15	Use not recommended

Supplied: Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose[®] packages of 1000; Prescription Paks of 40, available singly and in trays of 10.



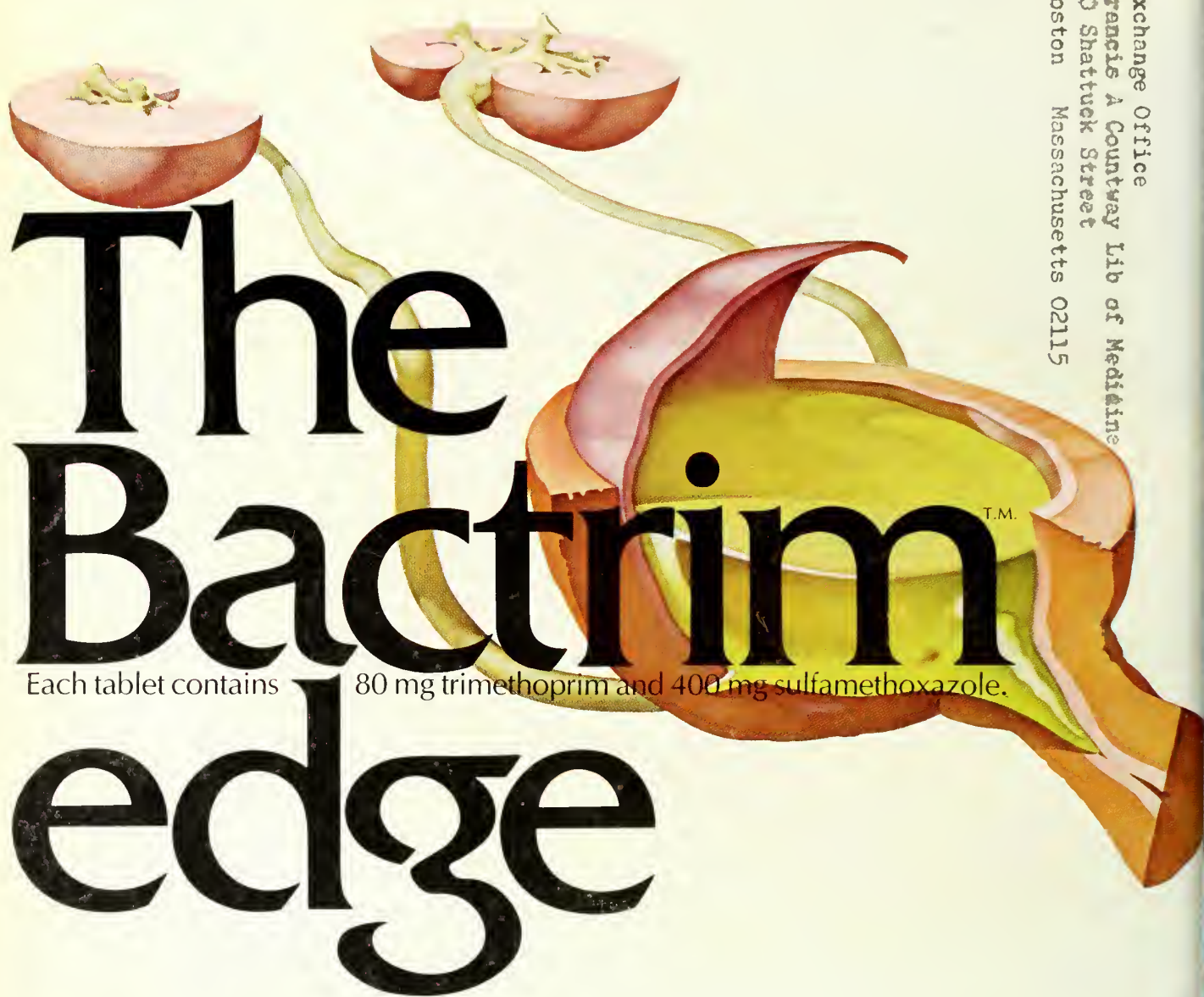
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THE JOURNAL

SOUTH CAROLINA MEDICAL ASSOCIATION

ULTRASOUND DIAGNOSIS

DIAGNOSTIC ULTRASOUND IN OBSTETRICS AND GYNECOLOGY

EMPLOYEE TUBERCULOSIS CONTROL

ORGANOPHOSPHATE POISONING

VOLUME 71

MAY 1975

NUMBER 5

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- Associated depressive symptoms

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Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor

neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

JUN 9 1975

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent

in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium[®] (diazepam) 2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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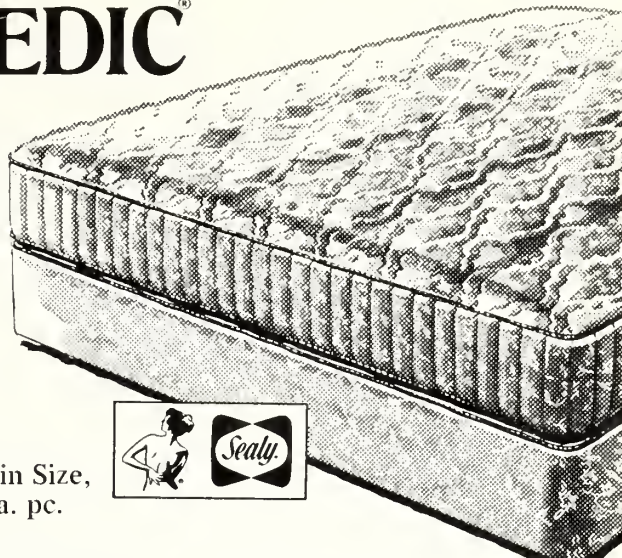
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THE JOURNAL

SOUTH CAROLINA MEDICAL ASSOCIATION

VOLUME 71

MAY, 1975

NUMBER 5

ULTRASOUND DIAGNOSIS — NEW DIAGNOSTIC TOOL FOR YOUR PATIENTS

U. HOYT BODIE, M. D.*

Ultrasound diagnostic studies involve the use of high frequency sound waves, beyond audible range, for the purpose of gaining useful information about a patient's medical diagnosis. This was developed during World War I, and it came into use as sonar during World War II, especially for locating submarines. Actually various animals such as porpoises and whales have been shown to be equipped with sonar; they can send out and receive sonic waves to locate fish and other objects.

After World War II, the principles of sonar were adapted for medical uses. The first commercial ultra-sonic equipment became available in the mid and late 1950's.

EXPLANATION OF EQUIPMENT

The basic machine (see figure 1) contains a pulse generator, an oscilloscope, a transducer, and electronic circuitry that amplifies and modifies the signals received. The electrical impulses, as produced by the reflected ultrasonic waves, are displayed on an oscilloscope and then recorded, using polaroid film, paper print-out, or x-ray film. A coupling agent is always necessary between the transducer

surface and the patient's skin to eliminate trapped air. Air is a very poor conducting medium for ultrasonic waves. We use a special aquasonic gel or mineral oil.

The transducer is the main production item of the equipment, and it contains a piezoelectric crystal that has special ability to contract and expand when pulsed electric current is applied. The rapid oscillation of the crystal results in sound waves beyond the range of human hearing (above 20,000 cycles per second). The waves strike an interface and are reflected back to the crystal.



FIGURE 1: ULTRASONOGRAPHY Machine which incorporates all three modes of diagnosis. Note polaroid camera for filming on far left, oscilloscope screen next to polaroid camera, large TV type screen for viewing examinations, transducer with piezoelectric crystal being held in technician's hand, and special ultrasonic scan gel which is used as a coupling agent. Paper print-out unit is not visualized.

*Chairman, Department Nuclear Medicine and Ultra-sound Diagnosis
S. C. Baptist Hospital, Columbia, South Carolina
February 1975

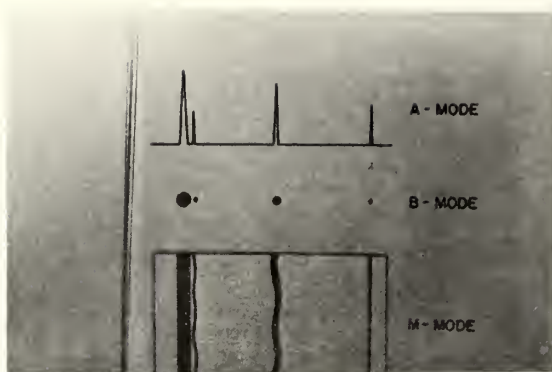


FIGURE 2: DISPLAY MODES FOR ULTRASOUND — schematic illustrations of A-mode, B-mode, and M-mode.

The transducers that are used in medicine vary in shape and size. The bell-shaped transducer is used for most diagnostic or medical procedures; the ophthalmologist uses a pencil-like transducer for measurements; there is a long thin one for direct vascular measurements.

When the ultra-sonic waves strike an interface, a portion of the beam is reflected, producing an echo. If the interface is perpendicular to the transducer, this echo will strike the piezoelectric crystal, resulting in an electrical impulse which is then displayed on the oscilloscope screen.

There are several ways in which the echoes may be displayed. (See figure 2.) The most common is known as A-mode in which it is displayed on the oscilloscope screen as vertical deflections from the horizontal baseline. The next mode is known as B-mode, and if one were to look down on the top of the spikes produced on the oscilloscope screen, one would see dots on end reflecting B-mode. The third mode is the M-mode display, and this is the echo pattern which results when the dots off the top of the B-mode are swept across an oscilloscope screen. Also time exposure photography can be done of the M-mode display.

ADVANTAGES OF ULTRASOUND

Ultrasound has many definite advantages as follows:

1. The patient has no pain to experience.

2. There is no danger from exposing the patient to sound waves.
3. No one has been able to prove in any way since ultrasound has been in use that any hazard results to the patient or to offspring. Extensive studies are being done along these lines for all of the regulatory agencies.
4. There is no evidence of radiation effect whatever.
5. The study requires no medication; amyl nitrite is given for an occasional echocardiographic study.
6. It is strictly a non-invasive procedure and does not require needle puncture as many x-ray and nuclear medicine studies do.

EQUIPMENT AND PERSONNEL

There are many commercial brands of equipment now on the market. We at present have a unit which has a potential for all three modes. Figure 1 shows you an overall view of the unit. You will note that it has two screens for viewing and filming. One of these screens is an oscilloscope and the other is a TV type screen. Our unit has the capability of polaroid or paper print-out, and we find the paper-print-out to be most useful and quite advantageous. The transducer arm is visualized, and this is actually the major part of the unit since it contains the small piezoelectric crystal at its end.

We also have a Doppler unit which is especially good for listening to the vascular sound of placenta and fetal heart tones. Also it is excellent for use in checking out vascular stenoses and occlusions in major vessels.

As previously indicated, there must be a very good coupling agent between the transducer surface and the patient's skin to eliminate trapped air. We use aquasonic gel or mineral oil.

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Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a

thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in

cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

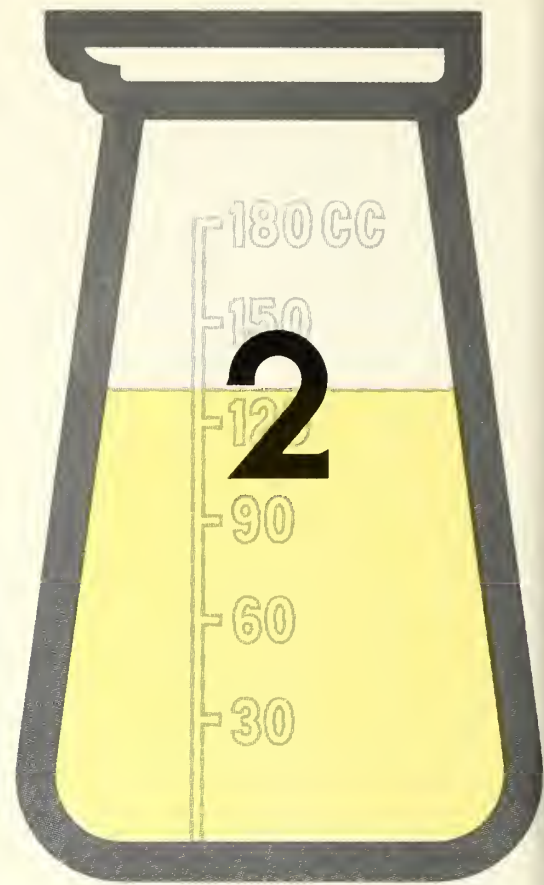
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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic non-obstructed urinary tract infections (primarily pyelonephritis, pyelitis, and cystitis) due to susceptible organisms. **Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials, including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, peri-orbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

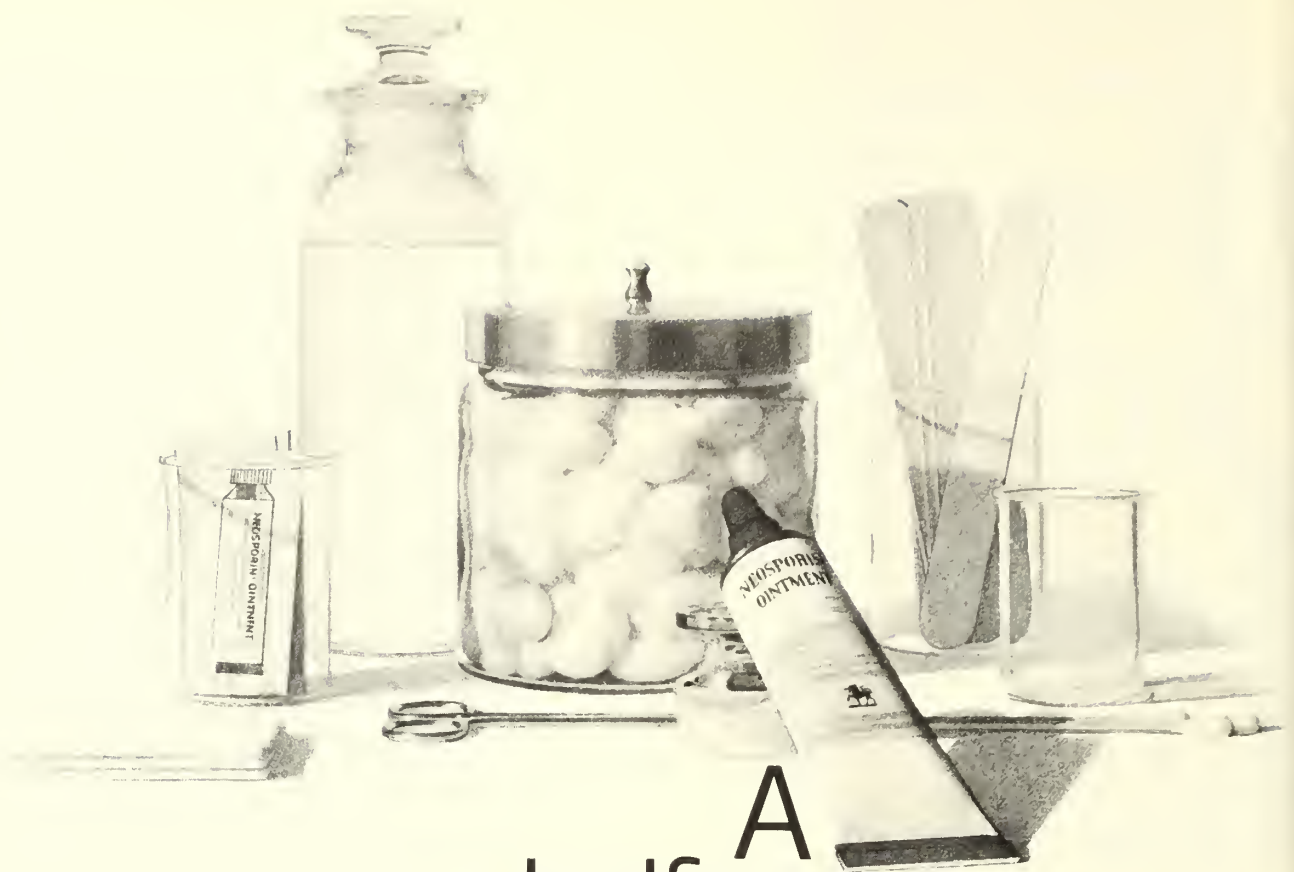
Usual child's dosage: 0.5 Gm (1 tab or teasp.) / 20 lbs of body weight initially, then 0.25 Gm / 20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg / 24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole / teaspoonful.



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Each gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs.
In tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.


WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of perst allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PM

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of the field. She also must have considerable knowledge of anatomy from the standpoint of transverse sections and tomography.

DIAGNOSTIC AND THERAPEUTIC USES

There are many diagnostic and therapeutic uses of ultra-sound. It seems that each day someone finds a new use for this mode of study. There are nine general use categories at present, and these are listed as follows:

1. Brain — Echoencephalography
2. Eye
3. Heart — Echocardiography
4. Obstetrics — Fetus and placentography
5. Gynecology — pelvic masses
6. Abdominal masses
7. Ascites and fluid
8. Major blood vessels — aneurysms
9. Therapy

BRAIN

The most commonly used diagnostic procedure with regard to the head is midline localization of the brain.

A-mode studies can be used to tell whether the midline structures are shifted to either side (see figure 3.) This is especially helpful in following patients with subdural hematomata or brain tumors. Also it should be pointed out that the brain is now being studied with very

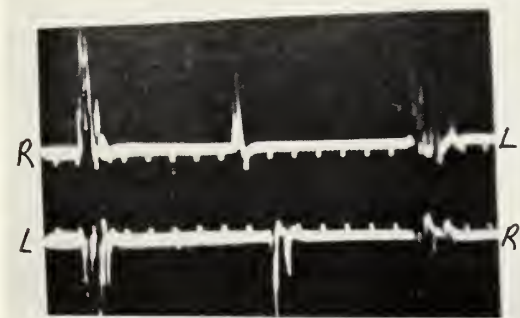


FIGURE 3: A-MODE STUDY for localization of midline brain structures. Sound waves are introduced from each temporal area of skull; a 6 mm. shift of midline echoes is formed in this patient. He had craniotomy done for a glioma in left parietal region of brain. Shift of midline structures shown here is from left to right.

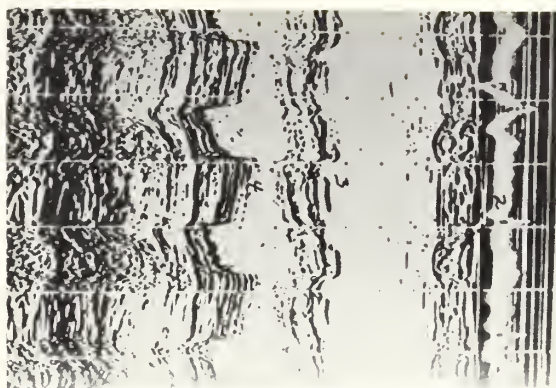


FIGURE 4: MITRAL STENOSIS — Typical findings on echocardiogram. 1. Entrance echoes on chest wall. 2. EKG Tracing. 3. Septal echoes. 4. Flattening of E-F slope on anterior leaflet of mitral valve.

highly specialized ultrasound equipment at many centers in the country. Detailed anatomy of ventricles and other brain structures can be obtained by this method.

EYE

Specialized transducers and ultrasound units have been set up in large medical centers that can give very minute and accurate detail of structures in the eyeball. Normal structures can be seen on A-mode studies, and foreign bodies as well as tumors can be visualized by special type B-mode scans.

HEART

Echocardiography has become a very valuable tool in all modern cardiology departments throughout the country. M-mode scans can be used to visualize pericardial effusions, all of the valves and chambers of the heart. Left atrial tumors can be quite well visualized by this method. A typical echocardiogram of a patient with mitral stenosis is illustrated in Figure 4.

OBSTETRICS — GYNECOLOGY

This specialty in medicine has perhaps taken better advantage of ultrasound diagnostic studies than any other specialty. Patients can be studied from early pregnancy all the way to term, and biparietal diameter measurements of the baby's head can be obtained with ultrasound. From the biparietal diameter measurements we can correctly predict the baby's



FIGURE 5: TWIN PREGNANCY from ultrasonic scan of maternal abdomen. 1. Head of twin #1. 2. Head of twin #2. 3. Apex of mother's bladder. 4. Anterior abdominal wall of mother. 5. Placenta with chorionic plate.

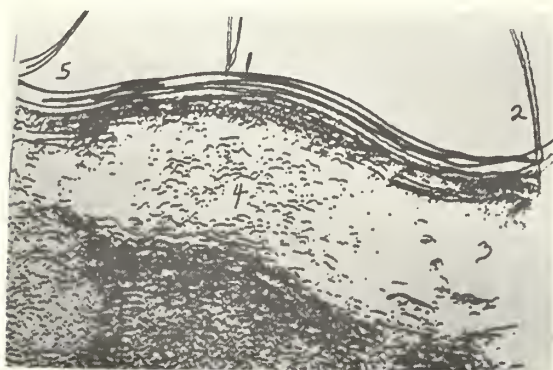


FIGURE 6: HYDATIDIFORM MOLE as shown on ultrasonogram of uterus. 1. Umbilicus. 2. Pubic symphysis. 3. Distended bladder. 4. Molar tissue echoes in uterus. 5. Xiphoid.

age to within one week. This is the most accurate method that we have to depict fetal age. Also it has the advantage of no radiation to the fetus or mother. The placenta can be well localized, and we can even visualize multiple pregnancies. (See figure 5 of twin pregnancy.) We also have been able to demonstrate anencephalic monsters by this method of study.

Tumors of the pelvic area such as dermoid cysts, fibromyomata, and ovarian masses can be visualized with ultrasonic techniques. Molar pregnancies produce a picture which is almost pathognomonic (see figure 6).

ABDOMINAL MASSES

Ultrasonography is especially good to visualize pancreatic cysts, cysts of the kidney, solid tumors of the kidney, and retro-peritoneal tumor masses.

ASCITES AND PLEURAL FLUID

Patients with ascites are often studied with ultrasound to determine where the fluid is and to approximate volumes. It is interesting to note how fluid shifts in the abdomen when the patient changes position. Pleural fluid can also be studied.

MAJOR BLOOD VESSELS

An excellent outline of the abdominal aorta can be obtained by means of ultrasonography. Aneurysms of the abdominal aorta can be accurately localized and very accurately measured in longitudinal and transverse dimensions. (See figure 7.) Using ultrasound technique to study major blood vessels for aneurysm formations has the advantage of visualizing the aneurysm when it does not have calcium deposits in it. These calcium plaques are necessary for an aneurysm to be seen on a plain x-ray film.

RADIATION THERAPY PLANNING

Recently transverse ultrasonograms have been used to get contours of different areas of a patient's body for radiation therapy planning. Contouring the body by this method is more precise and accurate than the old solder wire method.

TREATMENT

There are numerous conditions which show much promise in the future with regard to treatment of diseases with ultrasound. Already conditions like bursitis, muscular strain, and whip-lash injuries



FIGURE 7: ANEURYSM OF ABDOMINAL AORTA from longitudinal ultrasonogram of abdomen. 1. Xiphoid of sternum. 2. Lumen of aorta. 3. Aneurysm bulging from aorta. 4. Umbilicus. 5. Anterior abdominal wall.

are successfully treated with ultrasonic beams in physical therapy departments. Considerable work is being done in Germany and in this country with regard to the possibility of dissolving certain types of kidney stones with ultrasound. Dr. Barry Goldberg in Philadelphia has done a great deal of excellent work about puncturing cysts of the kidney, as well as pericardial effusion tapping, with specialized ultrasound transducers and equipment. Obstetricians are depending on ultrasound scans to guide them for amniocenteses after studies have been done to localize the placenta.

FUTURE OF ULTRASOUND DIAGNOSIS

The future of this diagnostic mode of examining patients is unlimited. Already equipment which was purchased as little as a year ago is now out-moded by more modern equipment that will do studies in much greater detail. Machines are now being marketed that can produce what is called "gray scale"; this gives ultrasonic scans in various shades of gray, more

comparable to x-ray films than we have been able to get before. Also, prototype machines are being manufactured and studied in great detail using as many as 19 to 26 transducers to make motion picture studies with ultrasound technique. Babies in utero can actually be visualized kicking about with this technique, and it has been labeled "Real Time Ultrasonography."

SUMMARY

A brief discussion has been given with regard to the equipment and techniques necessary for ultrasonography. The multiple diagnostic procedures that can be done to good advantage for patients are discussed briefly. Specialists and general practitioners alike need to have knowledge of how these procedures can help them give better patient care. There is much potential for ultrasound diagnosis and treatment procedures in the future. The field seems to be unlimited, and it is growing so rapidly that it is a real challenge to keep up with the progress being made.

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DIAGNOSTIC ULTRASOUND IN OBSTETRICS AND GYNECOLOGY

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LINDA M. McCARTER*

Since the introduction of ultrasound for medical diagnosis in the 1950's, its use has progressed rapidly from an academic research tool to a mainstay of clinical practice. It is predicted that the medical applications of ultrasound will equal or even surpass those of x-rays within 10 years.¹ In the practice of obstetrics and gynecology diagnostic ultrasound has found multiple applications.

Ultrasound is simply high frequency sound waves. While audible sound waves vary from 25 to 18,000 cycles per second, frequencies used in diagnostic ultrasound vary between 500,000 and 20,000,000 cycles per second (20 MHz). In obstetrical and gynecological work, as in most abdominal ultrasound, waves of approximately 2.5 MHz are beamed from a transducer into the body under accurate directional control. A reflection or echo occurs whenever this beam strikes an interface between different types of tissues. These echoes can be translated into an image of the structures within the path of the sound beam.

Two methods of displaying ultrasonic information are used commonly in obstetrics and gynecology. In the A mode echoes appear as vertical spikes on a horizontal base line (Fig. 1). The distance or depth of any reflecting interface from the propagating source of sound waves is proportional to the time required for the echoes to return, and the distance between spikes indicates the distance between tissue interfaces. This mode is used primarily

in the measurement of the diameter of a fetal head or cystic mass.

In the B mode presentation (Fig. 2) echoes appear as luminous dots on an oscilloscope. The positions of the dots on the oscilloscope correspond geometrically to the positions of the reflecting inter-

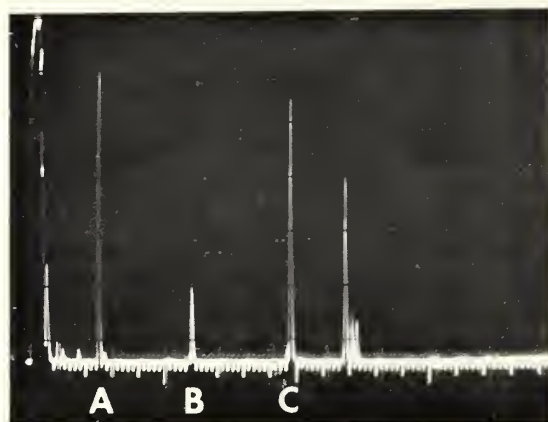


Fig. 1. Measurement of fetal biparietal diameter (BPD) by A-mode display. This BPD is 7.2 cm. A, anterior parietal bone; B, mid-line structure; C, posterior parietal bone.



Fig. 2. Pregnancy at 37 weeks gestation showing fetus in breech presentation. FH, fetal head; FB, fetal body; UE, upper extremity; LE, lower extremity.

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faces. By proper movement of the transducer in a scanning technique, a two-dimensional image of organs or tissues can be painted on the oscilloscope, and photographs of the image can be made for permanent records.

The pregnant uterus is a nearly ideal subject for ultrasonic study. As the uterus enlarges, the strongly sound-reflecting loops of bowel are forced out of the pelvis and away from the area of investigation. Earlier in pregnancy a full urinary bladder lifts both the bowel and uterus out of the pelvis and provides a fluid-filled medium that readily transmits ultrasound. Amniotic fluid also is very trans-sonic, and strong echoes are returned from placental and fetal tissues. More importantly, diagnostic ultrasound creates no hazard for mother or fetus^{2,3,4} such as the ionizing radiation involved in x-ray examinations.

OBSTETRICAL APPLICATIONS

Uses of diagnostic ultrasound in obstetrics are listed in Table I.

Early pregnancy: Intrauterine pregnancy can be detected as early as 5 weeks after the onset of the last menstrual period (LMP).^{5,6,7} By 7 weeks of amenorrhea the gestational sac is readily demonstrable (Fig. 3), and the diagnosis of pregnancy is quite easy to confirm. As the gestational sac enlarges and fills the uterine cavity, the ring structure disappears;^{3,8} this occurs about 11 weeks after the LMP. About the 13th or 14th week the fetal head becomes visible and should enlarge

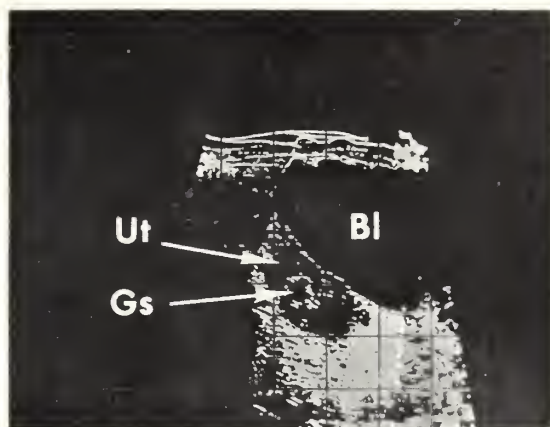


Fig. 3. Intrauterine gestational sac (GS) 40 days after last menstrual period. Ut, uterus; Bl, bladder.

progressively as gestation advances.

Fetal maturity: Gestational age can be determined with considerable accuracy from ultrasonic measurements. The fetal head size, or biparietal diameter (BPD), increases at a predictable rate during at least the last half of pregnancy.^{3,9,10,11,12,13} The fetal BPD is measured by ultrasonography (Fig. 1) and referred to a standard table which correlates fetal BPD with gestational age. Most studies report an accuracy within 7 to 14 days.^{9,11,13} Other fetal parameters, such as the thoracic diameter and cross-sectional area of the skull, have been measured in attempts to predict fetal body weight; these estimations have proved accurate within about 290-400 grams.^{9,14,15}

Multiple pregnancy: Twin gestational sacs have been detected as early as 7½ weeks menstrual age,⁶ and quintuplets have been diagnosed after only 9 weeks amenorrhea.¹⁶ Twins have been over-diagnosed in some scans because the fetal trunk or buttocks may resemble a second fetal head.⁶ In addition, twins have been overlooked, but careful scanning should prevent these errors (Fig. 4).

Fetal anomalies: Hydrocephalus (Fig. 5), anencephaly, polycystic kidneys, and ascites are among the fetal abnormalities which have been detected by ultrasonography.^{1,9} Most of these abnormalities have been found during scanning of a

Table I. Obstetrical Ultrasound

Normal pregnancy

1. Early pregnancy
2. Fetal maturity
3. Fetal lie

Abnormal pregnancy

1. Multiple pregnancy
2. Fetal anomaly
3. Polyhydramnios
4. Placental localization
5. Threatened abortion
6. Missed abortion
7. Hydatidiform mole

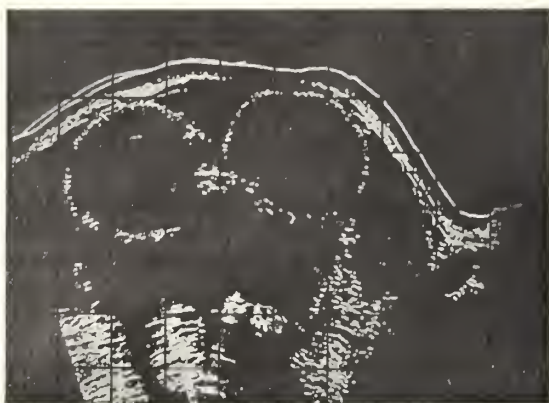


Fig. 4. Twin fetal heads at 31 weeks gestation.



Fig. 5. Hydrocephalic fetus at 36 weeks gestation. Fetal BPD 10.0 cm. FH, fetal head; Bl, bladder.

uterus which was either too large or too small for the stated period of gestation. It is reasonable to assume that meningo-myelocoele and gross limb deformities or absence also can be diagnosed by ultrasonography. A large echo-free space within the uterus indicates polyhydramnios (Fig. 6).

Placental localization: Ultrasound provides a rapid, simple, and accurate method of placental localization which has proved successful as early as 14 weeks gestation¹⁷ and appears to be more accurate than soft tissue placentography or radioisotopic scanning.^{17,18,19,20} This is particularly helpful in the evaluation of third trimester bleeding in which placenta previa (Fig. 7) must be considered and in the selection of a proper site for amniocentesis.

Threatened abortion: Ultrasonography is very helpful in the evaluation of bleed-

ing in early pregnancy. An absent, poorly defined, elongated, or fragmented gestational sac (Fig. 8) suggests the inevitabil-

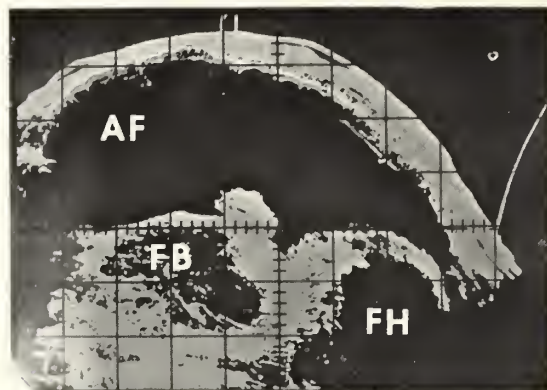


Fig. 6. Polyhydramnios at 31 weeks gestation. Large accumulation of amniotic fluid (AF) seen as echo-free space. FB, fetal body; FH, fetal head.

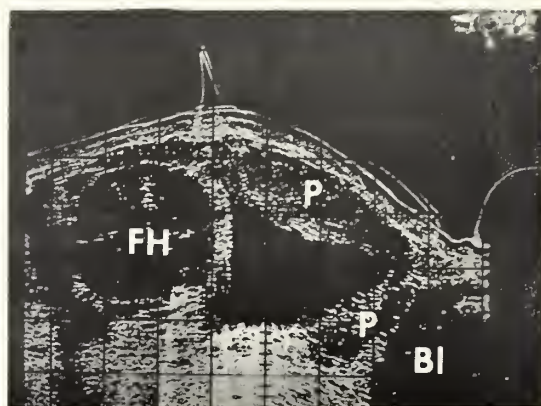


Fig. 7. Placenta previa at 35 weeks gestation. Placenta (P) seen anteriorly and interposed between maternal bladder and amniotic space. FH, fetal head.

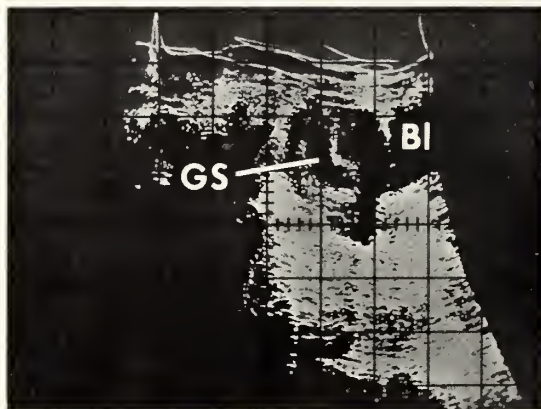


Fig. 8. Intrauterine gestational sac (GS) appears flattened, fragmented, and distorted. Spontaneous abortion occurred 2 days after this ultrasonogram was obtained. Bl, bladder.

ity of abortion.^{21,22} While implantation of the gestational sac in the lower uterine segment leads to a 60-70 per cent incidence of subsequent abortion,^{22,23} those low implantations which do not abort may lead to the development of placenta previa.²⁴ A failure of growth of the gestational sac or the presence of multiple disorganized intrauterine echoes may indicate missed abortion.

Hydatidiform mole: The ultrasonic diagnosis of hydatidiform mole depends on the presence of multiple fine speckled echoes which fill the uterus at high gain amplifications of the instrument but which disappear completely at low gain²⁵ (Fig. 9). This pattern is almost pathognomonic, and the correct diagnosis of hydatidiform mole never should be missed. However, leiomyomata and late missed abortions occasionally have been diag-

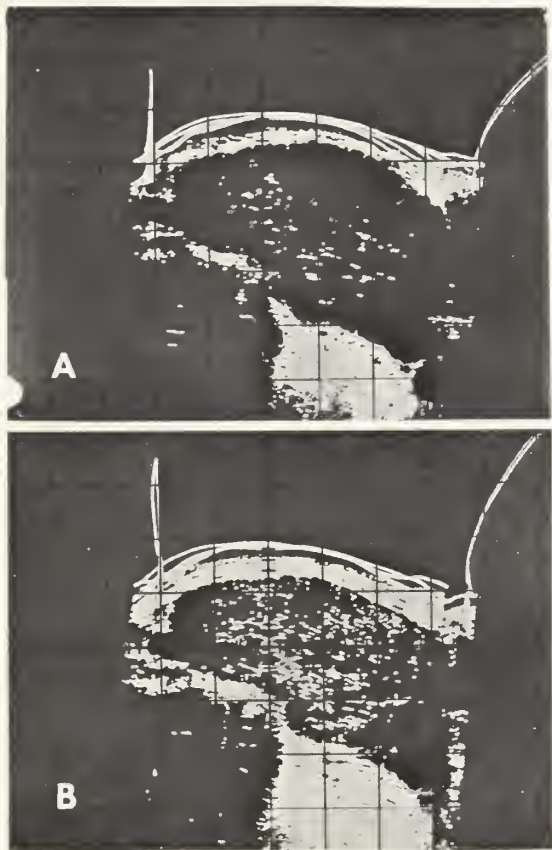


Fig. 9. Hydatidiform mole. A. Scattered fine echoes at low gain amplification. B. Fine echoes fill uterus at high gain amplification. This pattern said to resemble a snowstorm.

Table II. Gynecological Ultrasound

1. Pelvic tumors
2. Leiomyomata
3. Ascites
4. Response of malignancy
5. Intrauterine device localization
6. Ectopic pregnancy

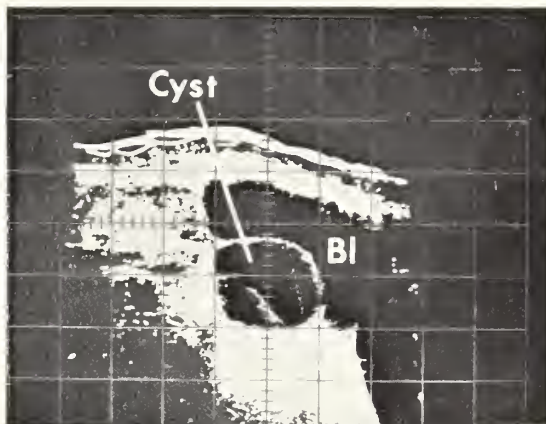


Fig. 10. Bi-locular thin-walled ovarian cyst measuring 5 x 6 cm. Bl, bladder.

nosed erroneously as moles.²⁶

GYNECOLOGICAL APPLICATIONS

Uses of ultrasound in gynecological diagnosis are listed in Table II. Applications in these areas have not been developed to the degree of those in obstetrics. These uses generally have involved the evaluation of pelvic masses. Uterine or adnexal origin of a mass can be determined, and differentiation between solid and cystic masses (Fig. 10) is usually simple.^{9,26} Although the ultrasonic echo patterns of some tumors has helped to establish the diagnosis of malignancy, differentiation between benign and malignant masses generally has been unsuccessful.^{26,27} Ultrasonograms can be used to follow the response of a tumor to irradiation or chemotherapy.²⁷ The diagnosis of ectopic pregnancy by ultrasonography is quite difficult.^{21,28} The ectopic pregnancy mass is usually heterogeneous and produces disorganized echoes; an intact ectopic gestational sac seldom is visualized.

PATIENTS AND RESULTS

Between November 1, 1972, and Decem-

ber 31, 1974, 1603 scans using a Picker Echoview IX ultrasonic laminography system have been performed on obstetrical or gynecological patients at the Medical University of South Carolina. The indications for these procedures are listed in Table III.

More than two thirds of the studies were done to determine or to confirm gestational age. Gestational age determination is done prior to any induction of labor or elective repeat cesarean section and in any patient in whom the uterine size is incompatible with the stated LMP. Many of the patients suspected of having twins fell in this latter group; that is, the uterine size exceeded that which was expected for the stated LMP. In the 70 scans done for suspected twins, 1 triplet pregnancy and 26 twin pregnancies were diagnosed. Twins were diagnosed erroneously in 2 patients, and 2 cases of twin pregnancy were overlooked.

All patients with uterine bleeding during the second or third trimester of pregnancy should be evaluated with ultrasonograms. Of 87 patients referred with the diagnosis of placenta previa, this diagnosis was confirmed in 12 cases, and 18

placentae were reported as low lying. Although not all of these low lying placentae have been confirmed at delivery, no case of placenta previa has been missed. One patient, who was diagnosed at 30 weeks gestation as having placenta previa, was delivered by cesarean section at 37 weeks, and was found to have a placenta which barely extended into the lower uterine segment. Placental migration²⁹ during development of the lower uterine segment may explain our failure to confirm placenta previa in this case. However, it seems most likely that the ultrasonic diagnosis was erroneous. We have been unable to diagnose abruptio placentae by ultrasound. Placental localization prior to amniocentesis has helped to lower our incidence of bloody taps.

Ultrasonography was used in the evaluation of 75 pelvic masses in which the difficulty lay in distinguishing uterine, ovarian, or tubal origin or in proving the cystic or solid nature of the mass. In addition, the presence of some masses which were suspected clinically was excluded by ultrasound. Many ovarian cysts have been managed conservatively after demonstration of apparently benign ultrasono-

Table III. Indications or referring diagnosis for ultrasonic scanning in obstetrics and gynecology at the Medical University of South Carolina.

	<i>Scans</i>	<i>Percent</i>
Gestational age determination	1091	68.2
Placental localization	156	9.7
Bleeding in pregnancy	(87)	(5.4)
Pre-aminocentesis	(69)	(4.3)
Pelvic mass	75	4.7
Suspicion of twins	70	4.4
Ovarian cyst	48	3.0
Threatened abortion	38	2.4
Fetal death	21	1.3
Leiomyomata	20	1.2
Pregnancy confirmation	19	1.2
Missed abortion	18	1.1
Hydramnios or anomaly	17	1.0
Hydatidiform mole	16	1.0
Ectopic pregnancy	7	0.4
Abnormal fetal lie	4	0.2
Lost intrauterine device	3	0.2
	<hr/> 1603	<hr/> 100.0

graphic characteristics and their lack of growth from one examination to the next.

Scans were done on 16 patients with clinical evidence of hydatidiform mole. Molar pregnancy was detected in 6 of these. One additional patient was diagnosed by ultrasound as having a molar pregnancy, but was found to have a missed abortion when suction curettage was performed.

CONCLUSIONS

The use of ultrasound in obstetrical and gynecological diagnosis is becoming increasingly valuable. Although some mistakes have been made, these mistakes

generally have been in interpretation rather than in the technique itself and should not detract from the value of the procedure. Most of our errors occurred early in our use of ultrasound and may reflect an over-eagerness on our part to make a "positive" or "outstanding" diagnosis when there was insufficient evidence on which to base such a diagnosis. As our diagnostic criteria have become more stringent, we have been able to place increased reliability on our ultrasonographic findings in the management of obstetrical and gynecological problems.

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EMPLOYEE TUBERCULOSIS CONTROL IN A PREDOMINATELY TUBERCULOSIS HOSPITAL

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MILDRED S. GIBSON, R. N.**

Soon after the South Carolina Sanatorium, the only state operated hospital for tuberculosis patients, came back under the administration of the State Board of Health in July, 1968, tuberculosis control measures for employees at the renamed State Park Health Center were increased from periodic chest x-rays to a plan of tuberculin testing and preventive treatment for tuberculin converters and reactors. The experiences and result of this program over a five year period are the subject of this report.

METHODS

The plan was for a standard intradermal tuberculin test (Mantoux), using 5 tuberculin units (TU) of PPD tuberculin, to be given to each new and current employee and to repeat this test on all negative or doubtful reactors at six month intervals on those with direct patient contact and at yearly intervals on those without direct contact. The tuberculin antigens used were PPD-S and subsequently PPD-T supplied by Communicable Disease Center and, in the last year, commercially available standardized PPD-T. A disposable plastic tuberculin syringe with 27 gauge needle was used for each test and the tests were given and read by the authors with few exceptions. In the initial period the atypical antigen PPD-B, also supplied by the Communicable Disease Center, was used to help determine specific sensitization in those with doubtful reactions, 5 to 9 mm of induration.

However, only those with 10 mm or more induration with 5 TU PPD-T were considered positive, or sensitized to human type tuberculo-proteins. The definition of conversion in the Tuberculin Testing Supplement to Diagnostic Standards (1969) was accepted, i. e., an increase of at least 6 mm from below 10 mm to 10 mm or above.¹ Also, following Diagnostic Standards, reactions from 0 to 4 mm were regarded as negative and those from 5 to 9 mm as doubtful. Tests were not repeated after a positive reaction was recorded with the exception of 15 instances in which there was conversion from 0 mm to above 10 mm within a year to determine the effect of preventive treatment in early converters on the degree of the tuberculin reaction. These tests were not counted in the tabulation of tests.

Standard 14 x 17 PA chest x-ray film on all new employees and on all current employees on their annual date of birth was routine at the time the new measures were undertaken. Those found to have a positive tuberculin or converted their tuberculin had a repeat 14 x 17 chest x-ray film unless their routine one was within the past month. A repeat x-ray film was obtained at the third, sixth, and twelfth month on those employees placed on preventive treatment with isoniazid. Following completion of treatment, employees were advised to have a chest x-ray film at any time that suggestive symptoms occurred, or if none, revert to annual date of birth for routine chest x-ray film.

Preventive treatment was considered for all those whose tuberculins were initially positive or converted their tuber-

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culin on subsequent tests. After determination that the chest x-ray film remained negative, or in some few instances with stable residues of old inactive tuberculosis, the reasons for preventive treatment and possible side effects and toxicity were discussed with the individual and, if accepted, a prescription was given for 100 isoniazid tablets, 100 mg. each, with directions to take one tablet three times daily for a few days and, if no untoward symptoms noted, to thereafter take all three tablets once daily after a meal. The prescription was filled by the hospital pharmacy and was refillable monthly for 12 months. They were advised to discontinue the isoniazid if any reactions or symptoms occurred which might be related to the medication and report to one of the authors for further evaluation. Everyone on preventive treatment was given an appointment for chest x-ray and clinical interview by a physician at the 3rd, 6th, and 12th month (on completion) of the treatment. Any indicated examination or laboratory screening was obtained at these times or at any time an employee reported suggestive symptoms, but none were done routinely.

Only a few tuberculin tests were done in the last half of 1968, thus the five year period covered by this report was essentially from January 1, 1969, through December 31, 1973, which was the cutoff date for this data. The plan, of course, continues in effect. There were a total of 950 tuberculin tests done during the five year period on a total of 449 individuals, varying from a single test to as many as 8 in some. Table 1 shows the numbers and percentages of negative, doubtful, and positive readings of these 950 tests. Table

TABLE 2

Status of 449 Persons Tuberculin Tested		
Reading	Number	Percent
Negative (0-4mm)	224	50.0 %
Doubtful (5-9mm)	46	10.2 %
Positive (10mm +)	106	23.6 %
Converters (Over 10mm by 6mm)	73	16.2 %
Total	449	100 %

2 shows the current tuberculin status of all current employees or at the time of resignation on those terminating employment. Half of the tested remain negative and the 106 reactors with the 73 converters makes a total of 179 or 39.9 per cent positive reactors. A still smaller group, 46, or 10.2 per cent had reactions in the doubtful range. The 73 converters deserve some further evaluation. This would appear to indicate a conversion rate of 16.2 per cent for the period or an annual rate of 3.2 per cent. Sixty-three of these converters were among the 250 employees with direct patient contact which would indicate a conversion rate of 25 per cent for the period or 5 per cent annually; there were only 10 conversions among the 199 without direct patient contact indicating a conversion rate of 5 per cent for the period, or 1 per cent annually. However, during this period the tuberculin antigen which was used was changed by the addition of Tween 80, a wetting agent, which stabilizes the strength of the solutions by preventing adherence of the antigen to the walls of the containing vials and syringes. Studies have shown rapid loss of antigen in preparations not containing such a stabilizing agent and many of the tests interpreted as doubtful with the earlier PPD preparations and subsequently positive as converters with the stabilized solutions may have been an artifact due to the loss of antigen in the earlier preparations.² There were 20 such instances among the 73 converters, 12 in patient contact employees and 8 among the non-contact. If these are then not in-

Results 950 Tuberculin Tests Given

Reading	Number	Percent
Negative (0-4mm)	683	71.9 %
Doubtful (5-9mm)	88	9.3 %
Positive (10mm +)	179	18.8 %
Total	950	100 %

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cluded, the conversion rates would change to 20.5 per cent for the period for contact employees, and 1.0 per cent for the non-contact, or an annual rate of 4.1 per cent and 0.2 per cent respectively. The conversion rate for the entire group would be 2.3 per cent annually which is 100 times the estimated infection rate for the population of the entire United States.³ However, it is less than one-tenth the infection rate reported among household contacts of newly reported active cases³ and is comparable to the 1.9 per cent reported in a general university hospital population and the 6.6 per cent among the 225 employees of the same hospital who had contact with infectious cases of tuberculosis.⁴

There were 13 employees tested who had a history or record of previously diagnosed tuberculosis and one of these became active again during the period. Seven had already received adequate drug therapy, including the one which reactivated. The remaining 6 were among those who received preventive treatment with isoniazid. There were 2 employees who developed new active tuberculosis during the period and one suspected of tuberculosis but subsequently diagnosis changed to pleurisy with effusion of undetermined etiology. These are briefly summarized.

Case 1: A 46-year-old B. M. housekeeping employee had 0 mm PPD 9-70 and 9-71. In February 1972 was admitted to VAH Columbia with diagnosis of alcoholism, diabetes mellitus and minimal active pulmonary tuberculosis on basis of slight RUL infiltrate and 20 mm PPD. All sputum smears and cultures were negative for afb and x-ray film completely cleared within three months. Chemotherapy consisting of streptomycin 1 gm. 3 x weekly, isoniazid 300 mg. and neopasalat 12 gms. daily was continued until 3-73 when SGOT elevated over 100 units (normal 40 units) and all chemotherapy discontinued. Patient was drinking excessively at this time and refused professional help with this problem and employment terminated in 4-73 for persistent absenteeism. He was referred to county health department of his residence for further follow-up.

Case 2: A 31-year-old B. F. nursing aide had negative chest x-ray film and 0 mm PPD 5-71. In January 1972 PPD was 20 mm and chest

x-ray film revealed a small pleural effusion on the right and she was admitted to the hospital for further study. Thoracentesis revealed clear yellow exudate which was negative on routine and afb culture. However, needle pleural biopsy revealed granulomatous reaction consistent with tuberculous pleuritis. She was discharged 2-9-72 with confirmed tuberculous pleurisy with effusion and referred to county health department for completion of chemotherapy. Five sputum examinations for afb were also negative by smear and culture.

Case 3: A 47-year-old B. F. housekeeping employee had negative chest x-ray film and 0 mm PPD 12-71, 2-72 and 11-72. Chest x-ray film 9-73 showed a small pleural effusion on right, but the PPD remained 0 mm. She was admitted to the hospital and thoracentesis revealed clear yellow exudate. Needle pleural biopsy was not diagnostic and routine and afb smears and cultures were negative. Sputum smears and cultures also negative for afb x 5. Discharged from hospital 11-73 with presumptive diagnosis of tuberculous pleurisy with effusion, not confirmed. She had returned to work continuing antituberculous chemotherapy. However, repeat PPD 2-74 remained 0 mm and chest x-ray film entirely negative. Hospital staff review of case resulted in change of diagnosis to pleurisy with effusion, etiology undetermined, and combined antituberculous therapy discontinued with recommendation to continue INH alone for 6 months.

Of the 179 employees with positive tuberculin including the 73 converters, 12 were not begun on preventive treatment with isoniazid for the following reasons: 6—history of adequate therapeutic or preventive treatment, 3—advised against by personal physicians, 2—history of hepatitis in recent past, and 1—employment terminated. For 167 reactors and 3 negative reactors preventive treatment was recommended; the 3 negative reactors being employees and household contacts of the employee who reactivated his disease. There were 34 positive reactors for whom preventive treatment was recommended but not carried out. It was declined outright by 8 and never started and the remaining 26 were begun but stopped the drug in less than three months for the following reasons: 5—orthostatic hypotensive effects (dizziness, vertigo, etc.); 4—hypersensitivity reactions (fever, malaise, skin rash); 4—advised to

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discontinue by personal physicians; 3—gastrointestinal disturbances; 2—skin rash only; 1—headache; 4—terminated employment and an additional 3, simply uncooperative. A total of 112 have completed their preventive treatment and 24 are currently continuing their treatment. Of those who have completed treatment 67 or 60 per cent picked up enough isoniazid by bottle count to have taken the drug more than 90 per cent of the time during the year. An additional 30 by the same evaluation took their pills at least 65 per cent of the time leaving only 15 or 13.4 per cent who took their isoniazid half of the time or slightly less. This is graphically illustrated in Table 3.

RESULTS

There were two new active cases and one reactivation during the five year period of this report. One of the new active cases was minimal pulmonary and one pleurisy with effusion, both converters at time of diagnosis; another pleural effusion remained tuberculin negative four months after the effusion and in absence of cultural or pathological confirmation was not felt to be tuberculous in etiology.

There have been no new cases of tuberculosis found among the 112 employees, including 50 tuberculin converters, who have completed their preventive treatment, nor in the 24 reactors and converters now continuing their treatment.

Reversion of the tuberculin skin test after preventive treatment with isoniazid was found in only 3 per cent of cases retested in the prophylaxis trials and, strangely, an equal number among the placebo group. Less than 10 per cent of positive reactors even showed a decrease in the size of reactions to below 10 mm, leading to the conclusion that isoniazid had little effect on established tuberculin sensitivity in man.⁵ Further analysis of data from these trials shows that, among household contacts, the protective effect of isoniazid was actually slightly better among those whose tuberculins did not convert than among those who did. This leads to the conclusion that isoniazid's ability to prevent disease was not related to its ability to produce reversion of the tuberculin sensitivity.⁵ There have been other studies which indicate that although there is little effect on established tuber-

TABLE 3

Drug Pick-Up Record for 112 Persons Completing Preventive Treatment

No. Persons	No. Tabs. Dispensed	% of Years Supply
4	400	37 %
5	500	46 %
6	600	55 %
8	700	64 %
7	800	73 %
15	900	82 %
27	1,000	91 %
40	1,100 +	100 % +

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TABLE 4

Effect of Isoniazid on Recent Tuberculin Converters (Under 12 Mos.)

Reactions After INH	No.	Percent
Reverted to Negative	4	26.7 %
Decreased Reaction	5	33.3 %
Unchanged Reaction	3	20.0 %
Increased Reaction	3	20.0 %
Total Retested	15	100.0 %

culous reactions of over a year's duration, there is a high degree of reversion among the very early converters—100 per cent in a U. S. Navy Study⁶ and 50 per cent in a university hospital group.⁴ In this study 15 of the employees who converted their tuberculin within a 6 to 12 month period, and who had picked up adequate supplies of isoniazid to have taken them regularly, were retested between 1 and 20 months after completion of their treatment. These tests were not counted in the tabulation of skin tests done. Table 4 shows the results. As can be seen 4 or 26.7 per cent reverted their tests to negative, while 5 or 33.3 per cent decreased their reactions by more than 2 mm. Three, or 20 per cent, were unchanged while 3, also 20 per cent, actually showed increase in size of reactions.

A review of hospital admissions for the five year period preceding this study revealed that there were also two new active cases of tuberculosis among employees from January 1, 1964, through December 31, 1968. In contrast to the two new cases for the last five years, both of these were pulmonary, one advanced and one minimal, and both confirmed by positive smears for afb and cultures for *M. tuberculosis*.

As stated earlier, no routine laboratory procedures were done during the year's medication with isoniazid; however, at any time symptomatic monitoring sug-

gested even possibility of toxicity, appropriate laboratory tests were done. There were 9 instances in which liver screens consisting of SGOT, SGPT and alkaline phosphatase were done. In seven, these tests were within normal limits. Only in one case did the SGOT and SGPT levels rise above 100 units (normal 40 units). This was in a black male in the 8th month of preventive treatment. The isoniazid was discontinued and the enzyme levels returned to normal in two months. The alkaline phosphatase was initially slightly elevated in this case also. The serum bilirubin was not elevated. In the other instance the elevation of SGOT and SGPT was under 100 units and isoniazid was continued after a brief interruption to completion of treatment with return of these enzyme levels to normal. Fasting blood sugar levels were abnormal in one and normal in two others, all known diabetics. Complete blood counts were normal in three instances and in one showed only slightly lowered hemoglobin level. In this case an iron preparation was given for a month with return of hemoglobin to normal range while continuing isoniazid.

Concurrent diagnoses of hypertension were noted in 17 employees, Diabetes Mellitus in 4, Arteriosclerotic Heart Disease in 1, Chronic Obstructive Pulmonary Disease in 1, and Rheumatic Cardiac Valvular Disease in 1. None of these seemed

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to present any problems with preventive treatment except for one hypertensive who could not tolerate isoniazid because of severe orthostatic hypotensive effect. Even switching to a bedtime dosage schedule, a maneuver which makes it possible for most patients with mild orthostatic hypotensive effects to continue their isoniazid, was unsuccessful in this case.

The need for a tuberculosis control program for employees is not limited to a predominately tuberculosis hospital. This can be readily substantiated by reviewing the 536 admissions to the tuberculosis section of State Park Health Center for the year 1973. Two hundred (200), or 37.3 per cent, were initially admitted to general hospitals throughout the State with transfer to this facility after presumptive or definite diagnosis of tuber-

culosis had been made. Seven additional patients were seen in the emergency rooms of general hospitals where diagnosis of tuberculosis was made on basis of x-ray examinations and in some instances finding of afb in sputum smears. Of course the probability of spread of infection to others is greatest in those contagious cases undergoing diagnostic studies before the disease is known, when protective measures can be instituted. There is also a national trend to utilize the general hospitals for diagnosis and institution of therapy for tuberculosis patients, a practice which has already begun informally in South Carolina. It is therefore urged that every hospital adopt a similar or modified tuberculosis control program for their employees as a good industrial health practice.

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HYPOTHERMIA IN ORGANOPHOSPHATE POISONING AND RESPONSE TO PAM

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Physicians serving agricultural areas have become aware of the symptoms, signs and treatment of organophosphate (O-P) poisoning since the banning of DDT due to its persistence and buildup in the ecologic chain. Most poisonings arise from pesticides used in agriculture although O-P poisoning can occur from non-agricultural materials. Physicians have recently become more aware of the signs and symptoms of organophosphate poisoning; however, hypothermia is not mentioned as a possible sign by emergency treatment charts or publications. The following case illustrates both a non-agricultural source of poison and hypothermia.

CASE HISTORY

A 16-year-old white male was seen in a hospital emergency room February 2, 1974, because of abdominal cramps, nausea, vomiting, generalized weakness, muscle twitching and apprehension. About 90 minutes earlier, he had taken a full swallow of a mange-mite medication prescribed by a veterinarian for his dog, mistaking it for cough medicine.

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The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

On physical examination, his blood pressure was 152/102, pulse 96 and thready, respirations 24, rectal temperature 94.2 F. He was nervous, apprehensive but oriented with cold dry skin, constricted pupils and fine generalized muscular twitching, but no other neurologic abnormalities.

While in the emergency room, gastric lavage of 4 liters was done and 1 mg. of atropine I.V. given. On transfer to ICU, respiration had increased in rate and depth; skin was warm and slightly diaphoretic, muscle twitching increased and he complained of double vision. Emesis persisted. Four and one-half hours after admission, he was listless, apathetic but oriented, and hypothermia which lasted for at least 2 hours (94.2 and 94.8 R) was no longer present.

Blood analysis by the Chemistry Department of South Carolina Medical University showed a plasma cholinesterase level of 0.3 micromoles per minute (normal 2-4), RBC cholinesterase 1.1 (normal 10-20) by pH stat analysis. Twenty-four hours later, levels were 0.8 and 12.7 respectively.

After consultation with the Preventive Medicine Section of MUSC, he was given PAM, 1 gm. in 250 cc. of 5 per cent dextrose in water, I.V. over a 15 minute period, with this dose repeated in an hour. He was also started on 1-2 mg. of atropine I.V. 15 minutes, using tachycardia of > 140 and dilatation of pupils as guidelines. One hour after starting this regimen, the patient was more alert. Hand grip which has been grossly 10 per cent of normal (without evidence of respiratory muscle weakness) had returned to normal and abdominal cramping was much improved. Atropine was then continued on an hourly basis for a total of 50 mg. over a 48 hour period. The day after admission, he began to have inappropriate responses to questioning and subsequently hallucinations with pulse rates of 90-100. Atropine was continued and he was sedated with small doses of Thorazine. The following morning, he was drowsy but oriented to time, place and person. Pupils were dilated but of equal size and reactivity. Full history at that

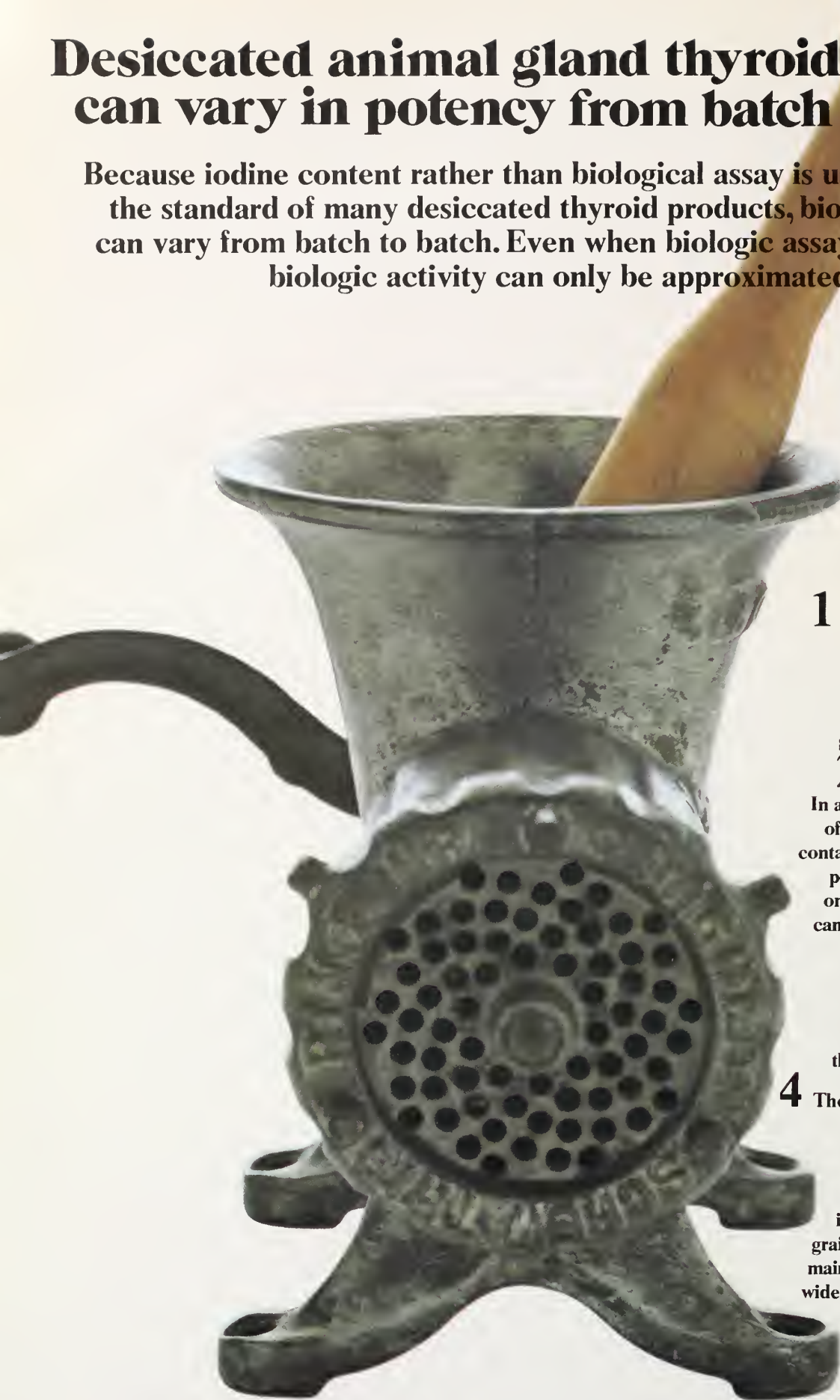
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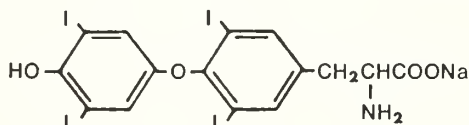
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Description

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Sodium Levothyroxine

Actions

SYNTHROID (sodium levothyroxine) **Tablets**, taken orally, provide hormone that is readily absorbed from the gastrointestinal tract. SYNTHROID **Injection** is effective by any parenteral route. Following absorption, the synthetic L-thyroxine provided by SYNTHROID products cannot be distinguished from L-thyroxine that is endogenously secreted. Each is bound to the same serum proteins and each exhibits a six to seven day circulating half-life in the euthyroid individual.

Both SYNTHROID products will provide L-thyroxine as a substrate for physiologic deiodination to L-triiodothyronine. Therefore, patients taking SYNTHROID products will demonstrate normal blood levels of L-triiodothyronine even when the thyroid gland has been surgically removed or destroyed by radioiodine. Administration of levothyroxine alone will result in complete physiologic thyroid replacement.

Indications

SYNTHROID (sodium levothyroxine) products serve as specific replacement therapy for reduced or absent thyroid function of any etiology. SYNTHROID **Injection** can be used intravenously whenever a rapid onset of effect is critical, and either intravenously or intramuscularly in hypothyroid patients when the oral route is precluded for long periods of time.

Contraindications

There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis. (See WARNINGS)

Warnings

Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions

Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule. With SYNTHROID (sodium levothyroxine) **Tablets**, the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

Adverse reactions

Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration

For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0.2 mg) of SYNTHROID (sodium levothyroxine) **Tablets** daily will restore normal thyroid function and only occasionally will patients require larger doses. Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism, special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent onset of hypothyroidism, full replacement dose of 150 mcg (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view of the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patient as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedematous infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 mcg (0.025 mg) per day. Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at three to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration.

Laboratory tests to monitor thyroid replacement therapy are of limited value. Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with the clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occurs and should not be considered evidence of overdosage per se.

In all cases, clinical impression of the well-being of the patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critical importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size, the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROID **Injection** may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsiveness within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred. Like the oral dosage form, SYNTHROID **Injection** produces a predictable increase in the circulating level of hormone with a long half-time. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient is fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

SYNTHROID **Injection** by intravenous or intramuscular routes can be substituted for the oral dosage form when ingestion of SYNTHROID **Tablets** is precluded for long periods of time.

How supplied

SYNTHROID (sodium levothyroxine) **Tablets** are supplied as scored, color-coded compressed tablets in 6 concentrations: 25 mcg (0.025 mg)—orange . . . 50 mcg (0.05 mg)—white . . . 100 mcg (0.1 mg)—yellow . . . 150 mcg (0.15 mg)—violet . . . 200 mcg (0.2 mg)—pink . . . 300 mcg (0.3 mg)—green. Depending on strength, these tablets are available in bottles of 100, 500, 1000 and 5000.

SYNTHROID (sodium levothyroxine) **for Injection** is supplied in 10 ml vials containing 500 mcg of lyophilized active ingredient and 10 mg of Mannitol, U.S.P. A separate 5 ml vial containing Sodium Chloride Injection, U.S.P. is provided as a diluent.

Directions for reconstitution

Reconstitute the lyophilized sodium levothyroxine by aseptically adding 5 ml of the Sodium Chloride Injection, U.S.P. to the vial. Shake vial to insure complete mixing. **Use immediately** after reconstitution. Discard any unused portion.



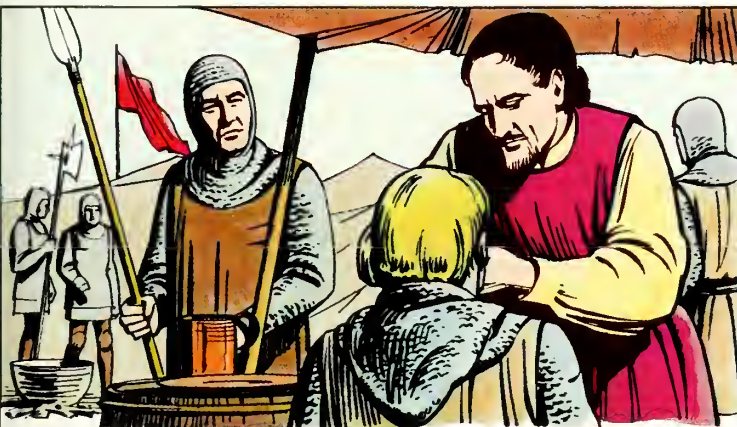
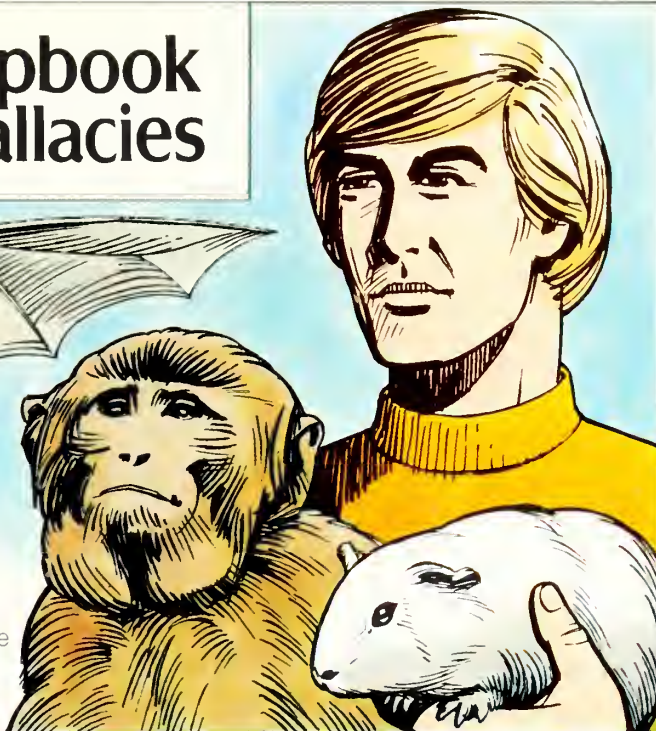
FLINT LABORATORIES
 DIVISION OF TRAVENOL LABORATORIES, INC.
 Deerfield, Illinois 60015

*U.S. Pat. 2,889,363

The **ALLBEE with C** Scrapbook of Vitamin Facts & Fallacies

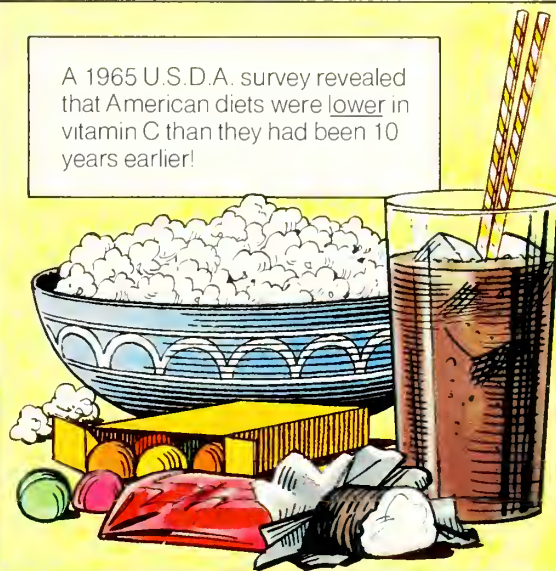


The Indian fruit-eating bat, almost all monkeys, man and the guinea pig are the only mammals whose bodies lack an enzyme needed to synthesize ascorbic acid from glucose! Hence they must obtain their vitamin C from exogenous sources.



De Joinville writing about a 13th century crusade reported that barber surgeons had to "cut away the dead flesh from the gums to enable people to masticate their food." The disease he described was probably scurvy.

A 1965 U.S.D.A. survey revealed that American diets were lower in vitamin C than they had been 10 years earlier!



The outer leaves of cabbage and brussels sprouts contain more vitamin C than the heads. Yet, ironically, these are often trimmed away by the grocer to improve appearance and enhance sales appeal! Many housewives trim them even more before cooking!

Available on your
prescription or
recommendation

ALLBEE with C

High Potency
B-Complex and
Vitamin C
Formula



A.H. Robins Company, Richmond, Va. 23220 **A.H. ROBINS**



Spasm reactor?

Donnatal!

	each tablet, capsule or 5 cc. teaspoonful of elixir (23% alcohol)	each Donnatal No. 2	each Extentab
hyoscyamine sulfate	0.1037 mg	0.1037 mg	0.3111 mg.
atropine sulfate	0.0194 mg.	0.0194 mg.	0.0582 mg
hyoscine hydrobromide	0.0065 mg	0.0065 mg.	0.0195 mg.
phenobarbital	($\frac{1}{4}$ gr.) 16.2 mg	($\frac{1}{2}$ gr.) 32.4 mg.	($\frac{3}{4}$ gr.) 48.6 mg
(warning: may be habit forming)			

Brief summary. Adverse Reactions: Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Contraindications: Glaucoma; renal or hepatic disease; obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); or hypersensitivity to any of the ingredients.

A·H·ROBINS A·H·Robins Company Richmond Virginia 23220

ORGANOPHOSPHATE POISONING

time revealed he had taken THC capsules (Tetrahydrocannabinol) some 24 or 48 hours before admission, but no other drugs at that time, though he had used marijuana as well as other drug substances of unknown type at school in the past. It was felt that the hallucinations reflected in part the atropine therapy, but the effect of other drug substances in causing them could not be entirely ruled out. His mental status cleared within 12-18 hours of discontinuance of atropine and he was discharged without residuals five days after admission.

The ingested material was identified as Dermaton, containing 25 per cent organic phosphate as an active ingredient with an LD 50 of 7 mg. per kilogram for mice. Gas chromatography of the patient's blood gave results identical to Dermaton.

DISCUSSION

The usual signs, symptoms and treatment of O-P poisoning are listed in Tables 1 and 2. Major problems in diagnosis and

treatment arise from a) lack of history exposure or knowledge of the type of poison involved, and b) reluctance to initiate treatment with atropine in sufficiently large and frequent enough doses. Detailed discussion of diagnosis, management and precautions was presented in 1972.¹

Experiments in 1968 and 1971 in the Netherlands showed that rats, given sublethal doses (10% or fewer rats died) of di-isopropyl phosphorofluoridate (DFP), a cholinesterase inhibitor, developed hypothermia with rectal temperatures dropping by 5-6 C° within 2 hours. The mechanism was felt to involve lowering of the hypothalamic heat regulating thermostat to give peripheral vasodilatation and reduced heat production from a

Table I
Symptoms and Signs

Mild - Moderate	Severe
Anorexia—nausea—vomiting Abdominal cramps, ± diarrhea Sweating, salivation, tearing Headache, constricted pupils Muscle weakness	Mental confusion, muscular twitching Pulmonary edema, shock, arrhythmias Convulsion, coma Respiratory paralysis Hyperthermia — mild or Hypothermia — moderate

Table II
Treatment

Mode	Dosage	Precautions
Maintain respirations. Gastric lavage—if ingestion. Total body bath—if skin absorption. Atropine.		(Respiratory collapse most serious effect of O-P).
	2 mg. q 10 mins. I.V. till pupils dilate or heart rate is 120-140, dry skin. Then 1 mg. q 1-4 hrs. or oftener, to maintain mild atropinization 48 hrs. or more.	Relieve cyanosis first to avoid ventricular fibrillation.
Protopam® (PAM)	1 gm. I.V. (< 500 mg./min.) Repeat in 1 hr. if no effect/muscle weakness. (Children 25-50 mg/kg.)	Harmful with carbamate poisoning. Use atropine alone. Little to no help if 36-48 hours after poisoning.

ORGANOPHOSPHATE POISONING

decrease in liver metabolism. Treatment with oximes similar to Pralidoxime chloride (PAM: pyrodine-2-aldoxime methiodide) 1 hour after poisoning by DFP lessened the intensity of the hypothermia by 1-2° C, with return toward normal at the same rate as in the untreated rats.² PAM has its maximum effect at the neuro-muscular junction and is felt to have little if any effect on the CNS.³ Temperatures were:

1130	94.2 R
1200	94.3 R
1400	94.6
1545	PAM started
1600	96.0
1700	97.0
1800	98.0

The rise in temperature in our patient cannot be attributed to PAM, however, directly related is the rapid return of grip strength. Atropine does not act to restore neuro-muscular function and a fully atropinized patient may die because of weakness of respiratory muscles.³

Avoidance of overatropinization can be difficult if rigid schedules are adhered to especially when the problem of drug usage arises. In this case, mental changes

were present with pulse rates of 90-100. In cases of mental or behavioral abnormalities in patients on maintenance atropine schedule, discontinuance of atropine with close monitoring of muscle strength would be indicated. Patients with continued muscular weakness would require a more rigid schedule, such as 1 mg. *q* hour until adequate recovery of voluntary muscle function occurs.

CONCLUSION

Organo-phosphate poisoning can occur outside of agricultural settings from non-agricultural materials. Hypothermia, as demonstrated from our patient and animal experiments, can be one of the early presenting signs in moderately severe to severe O-P poisoning. It indicates marked CNS effect on the hypophyseal thermoregulatory mechanism. Mental aberrations and behavioral changes in a patient on maintenance atropinization should arouse suspicion of overatropinization. If muscle strength is grossly normal and pupils dilated or normally reactive, even though the cardiac rate is under 100, atropine should be stopped and the patient closely observed.

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3. Milby, T. H.: Prevention and management of organophosphate poisoning (Council on Occupational Health), *JAMA* 216: 2131-3, 1971.

The MUDRANES

Discreet formulations of four well regarded drugs for the relief of bronchial distress—Potassium Iodide, Glyceryl Guaiacolate, Aminophylline, Ephedrine with Phenobarbital (to lessen cardiac stimulation).



INDICATIONS: For the prompt symptomatic relief of bronchial asthma, emphysema and bronchiectasis. The Mudranes dilate the bronchi and liquefy mucus plugs. **DOSAGE:** Tablet; One tablet with a full glass of water 3 or 4 times daily as required. Divide tablet for child's dose. Elixir; Children, 1 cc for each 10 lbs. of body weight. May be repeated 3 or 4 times a day. Adult, one tablespoonful 4 times daily. All doses should be followed with a glass of water.

CONTRAINDICATIONS: Aminophylline/Theophylline is contraindicated in the presence of severe cardiac arrhythmias and patients with massive myocardial damage. Ephedrine, in presence of severe heart disease, extreme hypertension, and in hyperthyroidism. Phenobarbital, in porphyria and in patients with known phenobarbital sensitivity. Potassium Iodide, in pregnancy (to protect the fetus against possible iodine-induced depression of thyroid activity), in tuberculosis (produces gumma dissolution), and in acne; also in the presence of known iodide sensitivity. **PRECAUTIONS:** Aminophylline/Theophylline should be avoided in patients with massive myocardial damage and/or severe cardiac


arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdosage. Potassium Iodide: Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing anginal pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdosage. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

HOW SUPPLIED: Mudrane and Mudrane GG available in bottles of 100 and 1000 tablets; Mudrane-2 and Mudrane GG-2 in 100s; Elixir in pints and half-gallons.

Federal law prohibits dispensing without prescription.



WILLIAM P. POYTHRESS & COMPANY, INC., RICHMOND, VIRGINIA 23261



**Ortho announces
a unique,
broad-spectrum
anthelmintic
effective against
whipworm...**

new
Vermox TRADEMARK chewable
tablets
(mebendazole)

...and highly effective against roundworm, hookworm and pinworm in single or mixed infections



No dosage calculations — one simplified dosage,
regardless of weight or age[†]

whipworm, roundworm, hookworm and mixed infections:

1 chewable tablet b.i.d. for 3 consecutive days

pinworm: 1 chewable tablet

If the patient is not cured three weeks after treatment, a second course of treatment is advised.

highly effective

	Mean cure rates	Mean egg reduction
Whipworm	68%	93%
Roundworm	98%	99.7%
Hookworm	96%	99.9%
Pinworm	95%	— — —

simplicity of administration patients can take the tablet at any time.

It can be chewed, swallowed or crushed and mixed with food. No messy liquids to pour.

not a dye new Vermox* (mebendazole) chewable tablets will not stain clothes, teeth, feces, toilet bowls, etc.

convenient neither laxatives nor special diet required. Therapy does not interfere with daily activities.

well tolerated transient symptoms of abdominal pain and diarrhea have occurred
in cases of massive infection and expulsion of worms.

[†]Vermox has not been extensively studied in children under 2 years of age, and thus, the relative benefit/risk should be considered before treating these children. Vermox is contraindicated in pregnant women. (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Indications Vermox* (mebendazole) is indicated for the treatment of *Trichuris trichiura* (whipworm), *Enterobius vermicularis* (pinworm), *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed infections.

Efficacy varies in function of such factors as pre-existing diarrhea and gastrointestinal transit time, degree of infection and helminth strains. Efficacy rates derived from various studies are shown in the table below:

	Trichuris	Ascaris	Hookworm	Pinworm
cure rates mean (range)	68% (61-75%)	98% (91-100%)	96% —	95% (90-100%)
egg reduction mean (range)	93% (70-99%)	99.7% (99.5-100%)	99.9% —	— —

Contraindications Vermox is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

*TRADEMARK

Precautions **PREGNANCY:** Vermox has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since Vermox may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and administration The same dosage schedule applies to children and adults.

For control of trichuriasis, ascariasis, and hookworm infection, one tablet of Vermox is administered morning and evening on three consecutive days. For control of enterobiasis, a single tablet of Vermox is given.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

How supplied Vermox is available as tablets, each containing 100 mg of mebendazole, and is supplied in boxes of twelve tablets.

Ortho Pharmaceutical Corporation,
Raritan, New Jersey 08869



Doctor, we owe you money.

Because your Blue Shield claims do not reach us until an average of 53 days after date of your service. And after that, it may take us two weeks to process and pay the claim either directly to you, or to your patient, so he can pay you.

After reaching us, about 89.8 percent of the Blue Shield claims are paid within less than 30 days.

Who among you is fastest ? Who slowest ?

We examined the tardiness of claims filing, by specialities of practice, and found that, on average:

- ▶ Surgical claims do not reach us until 50 days after your last date of service.
- ▶ Anesthesia claims arrive in 34 days.
- ▶ X-ray and laboratory claims take an average of 48 and 65 days, respectively, to arrive at our door.
- ▶ Medical care claims take 54 days.
- ▶ Oral surgery claims take 48 days and obstetrical and gynecological claims take 46 days.

Of course these are averages, but where do you stand?

You gave prompt treatment. You can receive prompt payment by sending us your Blue Shield claims on the day you last gave service.

How about it, Doctor ? We owe you money.



**Blue Cross
Blue Shield**®
of South Carolina

Editorial

Ultrasound Diagnosis

The articles by Drs. Boette and Hoerger present in a clear and concise manner the current applications of ultrasound. Those who have had experience with this very sophisticated diagnostic tool recognize that its potential in these areas is unlimited and that its extension to other areas of diagnosis and evaluation offers exciting possibilities.

Certainly the two areas of greatest development and application at the moment are in the field of cardiology and the determination of fetal maturity. The information that can be gleaned from ultrasonic studies of the cardiovascular system is unbelievably extensive. The detection of aneurysmal dilatation in the thoracic and abdominal aorta allows a diagnosis of this abnormality at a time when surgical correction can be done with greater efficiency and with minimum encroachment and involvement of adjacent structures by the aneurysm.

One of the most difficult and formidable problems in obstetrics has been the assessment of fetal maturity at a time when the decision has to be made as to whether the infant is safer outside of its uterine environment than allowing the pregnancy to continue. An even more exciting aspect of assessment of the intra-uterine fetus is the monitoring of fetal growth patterns in patients with chronic hypertensive vascular disease, diabetes, and other conditions in pregnancy associated with retarded fetal growth and development. The substitution of ultrasound studies for x-ray studies has the obvious and distinct advantage of eliminating or minimizing exposure of the gonads to even small amounts of irradiation.

In spite of the fact that current data show no adverse effects induced by ultra-

sonic studies, there is still some concern by those involved in such studies that one must make such statements with reservation until more time has elapsed in the follow-up of patients having had ultrasound studies in the past. This observation clearly points out in this era of the increasing number of malpractice suits that the patient must be advised of the nature of such studies as well as the value of information that can be gained.

One of the more intriguing and exciting areas for future investigation would be the application of ultrasound for the detection of tumor masses prior to the time that they are evident on either clinical or x-ray examination. The value of this as it influences the prognosis if neoplastic disease is of tremendous importance. Additional important information could be obtained in using ultrasound to follow patients with malignant disease in order to detect metastatic foci in the early stages. It could be used to quantitate the effectiveness of chemotherapeutic agents on tumor masses not accessible by manual measurement.

As with other sophisticated diagnostic modalities, interpretation of improperly recorded silhouettes results in inaccurate information. A thorough knowledge of the clinical problem and desired information is essential. To accept ultrasonic data as a single parameter of assessing a given problem is hazardous. Minor variations in angle of sound projection results in morbid image distortion.

In summary, ultrasound is now and will be even more an important diagnostic tool. One deterrent to availability at the moment is the cost of the unit. With increased application induced by increasing knowledge of its use, the cost will be justified.

E. J. Dennis, M. D.



Take your C.M.E. by the sea


**49 Continuing Medical Education courses at
AMA's Annual Convention, June 14-18, 1975
Atlantic City, New Jersey**

Those 49 Category I Continuing Medical Education courses are the largest number ever offered at an AMA convention. On top of that, there'll be Category I symposia and medical motion pictures on a wide variety of specialties.

Also featured are a number of special interest programs: a two-day session on the Medical Aspects of Sports, a series of special courses on clinical pathology, and a joint program by the American Veterinary Medical Association and the AMA on diseases transmitted to man by household pets. Physicians' wives and families will be offered interesting programs co-sponsored by the AMA's Council on Scientific Assembly and the Woman's Auxiliary of the AMA.

**For more information, write:
Dept. of Circulation & Records, AMA,
535 N. Dearborn St., Chicago, IL 60610,**





Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo.*
- Usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg/kg/day in rabbits and 10 mg/kg/day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.


Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG 
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert[®]/25 (meclizine HCl) 25 mg. Tablets for vertigo*

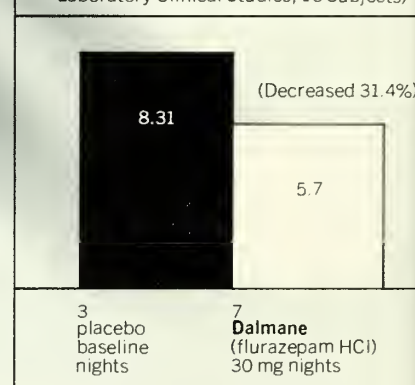


Would sleep with fewer nighttime awakenings benefit your patients with insomnia?

**Highly predictable results
for your patients with trouble
staying asleep...**

...can be obtained with Dalmane
(flurazepam HCl). As shown
below, Dalmane significantly
reduces nighttime awakenings:¹⁻⁴

Average Number of Nighttime Awakenings¹⁻⁴
(Four Geographically Separated Sleep Research
Laboratory Clinical Studies, 16 Subjects)



And for those with trouble falling asleep or sleeping long enough...

...Dalmane (flurazepam HCl) so delivers excellent results. Clinically proven in sleep research laboratory studies: on average, sleep within 17 minutes that lasts to 8 hours.⁵

Dalmane (flurazepam HCl) is relatively safe, seldom causes morning "hang-over"......and is well tolerated. The usual adult dosage is 30 mg *h.s.*, but with elderly and debilitated patients, limit the initial dose to 15 mg to preclude oversedation, dizziness or ataxia. Evaluation of possible risks is advised before prescribing.

REFERENCES:

Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971
Frost JD Jr: A system for automatically analyzing sleep. Scientific exhibit at the 124th annual Clinical Convention of the American Medical Association, Boston, May 29-Dec 2, 1970; and at the 42nd annual scientific meeting of the Aerospace Medical Association, Houston, Apr 26-29, 1971
Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly

or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

Depend on highly predictable results with

Dalmane[®]
(flurazepam HCl)

One 30-mg capsule *h.s.*— usual adult dosage (15 mg may suffice in some patients).

One 15-mg capsule *h.s.*— initial dosage for elderly or debilitated patients.

specifically indicated for insomnia

Objectively proved in the sleep research laboratory:

- sleep with fewer nighttime awakenings
- sleep within 17 minutes, on average
- sleep for 7 to 8 hours, on average, with a single *h.s.* dose.



ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
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Bioequivalence

Form with fields for data entry, including a date field and a signature line.

DATE	_____
SIGNATURE	_____



the weight of scientific opinion:

If the pharmacist substituted a chemically equivalent drug for the one you have specified for your patient—could you be certain of that product's safety and effectiveness simply because the chemical content was the same?

Definitely not, unless bioequivalence tests and other quality assurance checks had been conducted. The pharmaceutical industry and many scientists have maintained this position for years, but others have questioned it. Now the Office of Technology Assessment of the Congress of the United States has reported on the issue in its Drug Bioequivalence Study.*

Here are a few definitive statements in the O.T.A. report:

"...the problem of bioinequivalency in chemically equivalent products is a real one. Since the studies in which lack of bioequivalence was demonstrated involved marketed products that met current compendial standards, these documented instances constitute unequivocal evidence that neither the present standards for testing the finished product nor the specifications for materials, manufacturing process, and controls are adequate to ensure

that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.



"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and

(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or (c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...



Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

protecting the integrity of your prescription

The Upper Functional G.I. Disorder

The Pseudo-ulcer

Ulcer-like symptoms: no G.I. pathology



X-ray demonstrates normal stomach.

The patient is convinced he has an ulcer. However, symptoms are not quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient understand how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist.* Where milder cases may respond to counseling alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms.

In these cases, Librax as an adjunct can greatly contribute to the course of therapy. Its dual action can offer relief of both painful symptoms and excessive anxiety, because each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br. The antianxiety action of Librium® (chlordiazepoxide HCl) makes Librax exceptional among drugs for certain gastrointestinal disorders associated with excessive anxiety; the clidinium bromide (Quarzan™) component furnishes dependable antisecretory-antispasmodic action. Dosage is flexible; it may be adjusted according to your patient's requirements within the range of 1 or 2 capsules three or four times daily, up to 8 capsules daily in divided doses. Please consult the complete product information regarding precautions and adverse reactions.

*Rome HP, Brannick TL: Orientation and mechanism of functional disorders; clinicophysiology correlation, chap. 133, in *Gastroenterology*, edited by Bockus HL. Philadelphia, W. B. Saunders Company, 1965, p. 1116.

An adjunct in anxiety-related
upper functional G.I. disorders

Librax®

Each capsule contains 5 mg chlordiazepoxide HCl
and 2.5 mg clidinium Br.

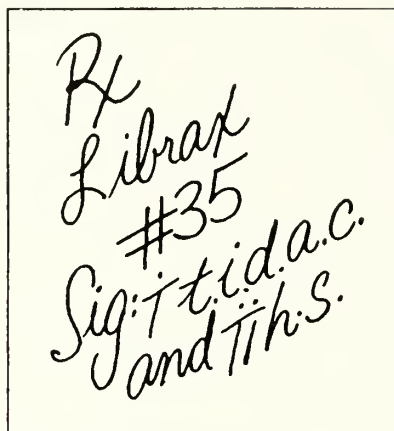
ROCHE

Please see summary of product information on following page.

An adjunct in anxiety-related
upper functional G.I. disorders

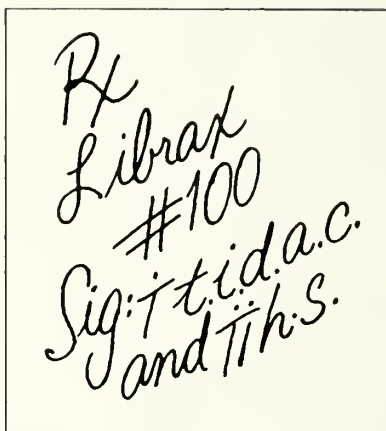
Librax[®]

Each capsule contains 5 mg chlordiazepoxide HCl
and 2.5 mg clidinium Br.



Initial therapy

The initial prescription allows evaluation of patient response to therapy.



Follow-up therapy

Follow-up therapy with a prescription for 2 to 3 weeks' medication usually helps maintain patient gains.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures

necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anti-coagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

Dosage: Individualize for maximum beneficial effects. Usual maintenance dose is 1 or 2 capsules, 3 or 4 times a day, before meals and at bedtime. Geriatric patients—see Precautions.

How Supplied: Librax[®] Capsules, each containing 5 mg chlordiazepoxide hydrochloride (Librium[®]) and 2.5 mg clidinium bromide (QuarzanTM)—bottles of 100 and 500.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

That's how **Business Week** talked about us. We're often compared with New England prep schools...and not just because of our rambling mountain campus and ivy covered buildings.

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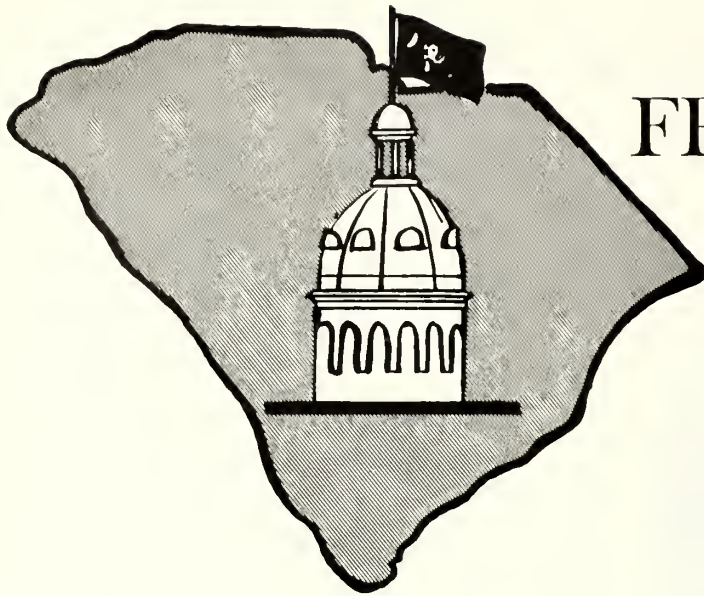
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FROM THE CAPITOL

DEXTER B. ROGERS, M.D.
CHAIRMAN, SCMA
LEGISLATIVE COMMITTEE

The most exciting news from the Capitol is the passage of a bill establishing a Joint Underwriters Association which can be enacted whenever the Insurance Commissioner considers an emergency need exists. Should physicians in the state find the absence of coverage or should rates due to lack of competition become unreasonably high, the JUA would become the exclusive provider for professional liability insurance to physicians.

This bill is effective only through December of 1977, so more permanent solutions are being sought. A study committee is being proposed in the House and the Senate to pool the knowledge of the doctors, insurance representatives, trial lawyers and legislators. Also, SCMA has had introduced four bills which should dramatically aid in solving the growing malpractice lawsuit situation: 1) S. C. Medical Disciplinary Act; to provide for a disciplinary mechanism through the SCMA under which every physician in the state would fall; 2) a reduction in the statute of limitations to two years instead of the current six, and to the age of eight in children rather than the age of majority as now exists; 3) an ad damnum clause which would prevent suing for a specified

amount; and 4) a contingency fee schedule which would reduce the attorney fee as the award increased.

Another bill is hoped to be introduced into the Senate which would limit the amount of money awarded on a medical malpractice suit to \$500,000 maximum. An individual physician would be liable for only \$100,000 and the remainder would be provided by a special State fund.

The legislature, particularly B. L. Hendricks, Jr., of Easley, and Jack Smith, of Hartsville, are to be commended and appreciated for the fine efforts on behalf of the people and of SCMA. The 1975 General Assembly has proved itself to be responsive to our needs and doctors should show their appreciation by contacting their legislators and thanking them.

We have had a great track record this year with no bill which SCMA opposed passing. Either they were defeated or forced into a satisfactory compromise. All bills that SCMA introduced or endorsed have moved quite well. Although the wheels of progress at the State House are very slow this year, a bill to make Medicaid payments equal statewide has passed, and some others have passed one body and await action in another. Hopefully, many of the bills of interest to

SCMA will be released with the flow that is expected toward the end of the session.

One amendment that SCMA wanted to introduce never materialized because no response came from the doctors. Many complaints were voiced about abuses regarding acupuncture, so SCMA approached B. L. Hendricks, Jr., about introducing an amendment which would place acupuncture in an accredited hospital permitting it, and with the coordination and review of the research area of the Medical University of South Carolina. SCMA was successful in obtaining letters from the S. C. Hospital Association and the MUSC stating their approval and ways to carry out this, but even after repeated attempts not one single physician was able to offer any evidence of any type of legal abuse caused by acupuncture. Mr.

Hendricks would not introduce such an amendment without good cause, so he suggested we attempt to gather such information and wait until the 1976 Session to introduce it. Gentlemen, we must respond to the inquiries from our legislative representative if we want to be successful in obtaining the type of legislation we feel we need. No one person can do a task of this magnitude.

Ron Harris, Director of Legislative and Public Affairs for SCMA mails a Legislative Report each week to the officers of the County Societies giving details of the activities at the State House. If you are not receiving this information from your officers at the County Society meetings, contact them and ask them to make this information available to all of the members.

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Rocky Mountain Spotted Fever Advisory

—By the S. C. Department of Health and
Environmental Control—

This is the time of year to increase the index of suspicion for Rocky Mountain Spotted Fever, also called tick typhus or American tick-borne spotted fever.

The South Carolina Department of Health and Environmental Control (DHEC) has observed a significant increase in the incidence of Rocky Mountain Spotted Fever in the state during the past 6 years. The first cases are usually reported in early May, with the peak number of cases coming in August.

Physicians are asked to be on the alert for febrile illnesses which follow tick bites or exposure in tick-infested areas. When Rocky Mountain Spotted Fever is suspected, serological confirmation is available from the Department of Health and Environmental Control Laboratory at 2600 Bull Street in Columbia. At least 2 serum specimens, collected 2 weeks apart, should be submitted to the State Laboratory in order to determine a rise in antibody titer. All cases should be reported to the DHEC Division of Epidemiology via the local county health department.

Severe headache, listlessness, myalgia, sudden chill, rapid rise in temperature and rash are characteristic symptoms of the disease and when a history of exposure to ticks is also present, the diagnosis is suggested. Symptoms may occur from two to twelve days after a person has been bitten by an infected tick. The distinctive rash usually appears on the extremities during the third day of the disease; early rash may resemble measles or other rash illnesses.

When diagnosed early, Rocky Mountain Spotted Fever can be treated successfully by the tetracycline drugs or chloramphenicol. Vaccines are available, but due to the questionable effectiveness of current vaccines and the low risk of contracting the

Rondomycin® (methacycline HCl)

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**

Usage in pregnancy. (See above **WARNINGS** about use during tooth development.) Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fetal growth rate observed in premature infants given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes, exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopical discoloration of thyroid glands, no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea. In uncomplicated gonorrhea, when penicillin is contraindicated, "Rondomycin" (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule: 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of "Rondomycin" (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia. 900 mg daily for six days.

Children—3 to 6 mg/lb./day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

SUPPLIED: "Rondomycin" (methacycline HCl) 150 mg and 300 mg capsules; syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev. 6/73



WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512



**When the focus is on bronchitis due to
susceptible strains of *H. influenzae* and pneumococci***

Rondomycin[®] 300 mg.
[methacycline HCl] Capsules

Delivers from the very first dose:

**Studies show that after the first dose serum levels rapidly rise above
minimum *in vitro* inhibitory concentrations**

*Since many strains are known to be resistant, routine sensitivity testing is recommended

disease, the vaccine is recommended only for special situations such as laboratory personnel working with *Rickettsia rickettsii* and persons whose occupations result in repeated exposure to ticks in endemic areas.

Only live ticks that are removed from human beings should be mailed to the following address to determine if the tick is infected with a rickettsial organism.

Division of Vector Control
South Carolina Department of Health
and Environmental Control
2600 Bull Street

Columbia, South Carolina 29201

Due to the large volume of ticks submitted, we cannot examine those removed from animals or the environment.

It is requested that all live ticks submitted be placed in a medicine vial containing a small strip of paper towel moistened with *one drop* of water. Attached information should include date, locality, host, collector and telephone number of physician or patient. The sender can expect a telephone reply if tests are positive.

If a positive tick was removed from a patient whose signs and symptoms are compatible with a diagnosis of Rocky Mountain Spotted Fever, treatment can be initiated.

Fifty-five cases of Rocky Mountain Spotted Fever were reported in South Carolina during 1974, including five fatal cases. The fatalities were two young girls, ages two and five; a 49-year-old woman, and a couple in their forties. More than three-fourths of the cases reported occurred in the Piedmont or above the fall line.

The American dog tick, *Dermacentor variabilis*, is the most prevalent tick in South Carolina and a potential carrier of tick-borne typhus. Not all ticks are infected. Even in heavily-infested areas, only about one tick in twenty is infective and, therefore, able to transmit Rocky Mountain Spotted Fever.

PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies* Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

ROERIG **Pfizer**

A division of Pfizer Pharmaceuticals
New York, New York 10017

NSN 6505-00-148-6967

**Pinworms, roundworms controlled
with a single, non-staining dose of**

ANTIMINTH[®]
(pyrantel pamoate)

equivalent to 50 mg. pyrantel/ml.
ORAL SUSPENSION

*Data on file at Roerig

Please see prescribing information on facing page



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faithfully for a long, long time. And when you're thinking of a second car for your family, you'd be hard put to find one more sturdy, more dependable, more sure on its feet, than your old Rolls-Royce.

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Pro-Banthine®

brand of
propantheline bromide

Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

Contraindications: Glaucoma, obstructive disease of the gastrointestinal tract, obstructive uropathy, intestinal atony, toxic megacolon, hiatal hernia associated with reflux esophagitis, or unstable cardiovascular adjustment in acute hemorrhage.

Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

Overdosage may cause a curare-like action, with loss of voluntary muscle control. For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and this possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evidenced by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

SEARLE

Searle & Co.

San Juan, Puerto Rico 00936

Address medical inquiries to: G. D. Searle & Co.
Medical Department, Box 5110, Chicago, Ill. 60680 481

"Antiacid" action for ulcer patients...

one of the many things you need in an anticholinergic.



Pro-Banthine is considered adjunctive in total peptic ulcer therapy that may include diet, conventional antacids, bed rest, and other supportive measures.

Pro-Banthine is provided in several different dosage forms which will meet virtually any clinical need. It is just as versatile in filling patient needs, among which are:

"Antiacid" action—Pro-Banthine® (propantheline bromide) reduces gastric secretory volume and resting total and free acid.

"Analgesic" action—Pro-Banthine helps to control the acid-spasm-pain complex.

Vigorous anticholinergic action—Pro-Banthine® Vials, 30 mg., are for intramuscular or intravenous use when prompt and vigorous anticholinergic action is required.

Mild anticholinergic action—Pro-Banthine® Half Strength, 7.5 mg. tablets, for more exact adjustment of maintenance dosage in mild to moderate gastrointestinal disorders.

Pro-Banthine® (propantheline bromide)

a good
option
in peptic
ulcer

In most cases of
sustained moderate hypertension,
ALDOMET[®] (METHYLDOPA|MSD)
usually offers more
than effective lowering
of blood pressure...



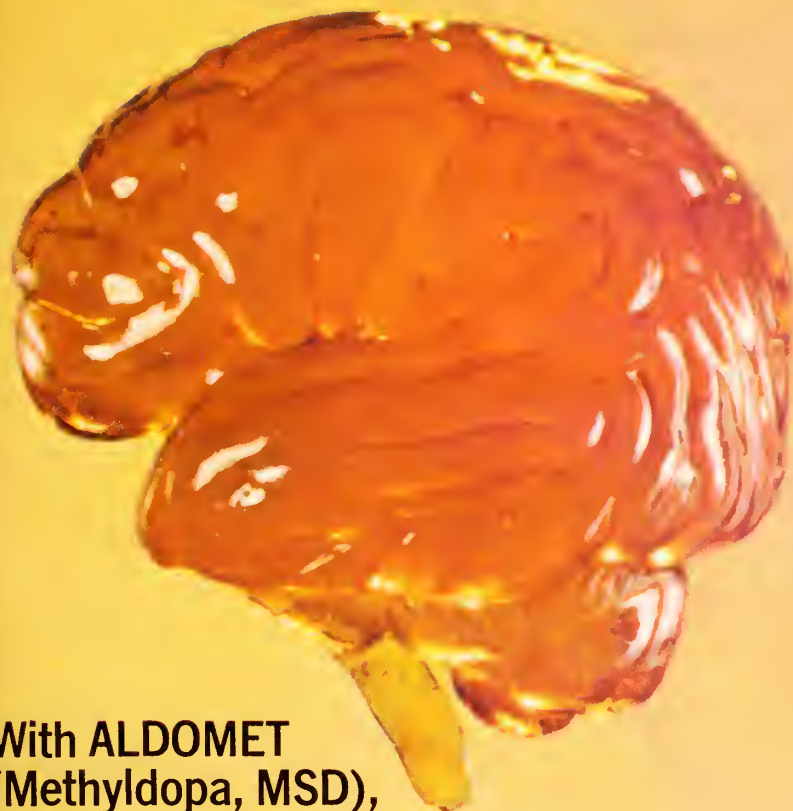
**With ALDOMET
(Methyldopa, MSD),
existing renal function
is usually unchanged**

ALDOMET has no direct effect on renal function. When used in effective doses, ALDOMET usually does not reduce glomerular filtration rate, renal blood flow, or filtration fraction.



**With ALDOMET
(Methyldopa, MSD),
cardiac output is
generally unchanged**

ALDOMET has no direct effect on cardiac function. When ALDOMET is used in effective doses cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is slowed.



With ALDOMET (Methyldopa, MSD), symptomatic postural hypotension is infrequent

ALDOMET reduces both supine and standing blood pressure. Less frequent symptomatic postural hypotension is experienced with ALDOMET than with many other antihypertensive agents. Exercise hypotension and diurnal blood pressure variations rarely occur.

for sustained moderate hypertension

TABLETS, 250 mg and 500 mg

ALDOMET[®]

(METHYLDOPA/MSD)

a unique antihypertensive agent

Contraindications include active hepatic disease and known sensitivity to the drug. Use with caution in patients with a history of liver disease or dysfunction. Not recommended in pheochromocytoma or pregnancy.

It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

For a brief summary of prescribing information, please see following page.

MSD
MERCK
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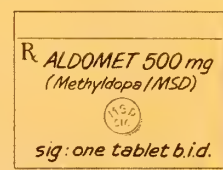
to further
simplify therapy
for many patients

now available
ALDOMET[®] 500 mg
(METHYLDOPA/MSD)

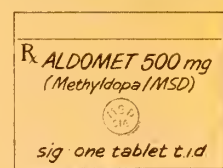
- often more practical to prescribe
- easier for patients to remember

Now offered in addition to the standard 250-mg tablet, the new ALDOMET 500 mg tablet is a patient convenience. An especially important one, since in hypertension convenience of the dosage schedule is one factor that can make the difference in compliance of the patient. The minimum daily dose of ALDOMET is 250 mg b.i.d. The usual starting dose is 250 mg t.i.d. Dosage is adjusted as necessary by adding or deleting 250 mg or 500 mg at intervals of not less than two days. The maximum dose is 3.0 g per day. Examples of b.i.d. or t.i.d. dosage convenience provided by ALDOMET 500 mg within the usual daily dosage range of 500 mg to 2.0 g:

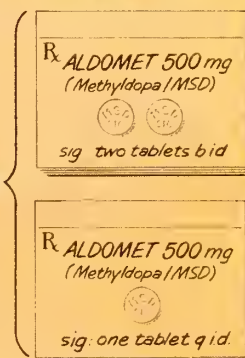
1.0-g
daily
dose =



1.5-g
daily
dose =



2.0-g
daily
dose =



NOTE: Tablets shown are not actual size.

in sustained moderate hypertension

ALDOMET[®] (METHYLDOPA|MSD)

usually lowers blood pressure effectively



Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis. Known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between six and twelve months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at six and twelve months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect

Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first six to twelve weeks of therapy or whenever an unexplained fever occurs. If fever, abnormalities in liver function tests, or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur.

Use in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Methyldopa may interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has occurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure are occasionally seen and include dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency. Angina pectoris may be aggravated. Symptoms of orthostatic hypotension may occur; if symptoms occur, reduction of dosage is suggested. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distention, constipation, flatulence, and diarrhea occur occasionally; these generally can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently and are relieved by administering a thiazide diuretic; if edema progresses or signs of pulmonary congestion appear, discontinue drug. A rise in BUN has been observed. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, Bell's palsy, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Note: Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Maximal recommended daily dose is 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

How Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

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Precautions:

ORAL: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six.

INJECTABLE: Keep patients under observation, preferably in bed, up to three hours after initial injection; forbid ambulatory patients to operate vehicle following injection; do not administer to patients in shock or comatose states; use reduced dosage (usually 25 to 50 mg) for the elderly or debilitated and for children age twelve or older.

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precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduc-

tion; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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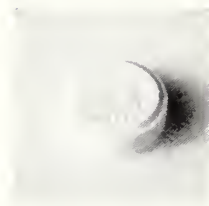
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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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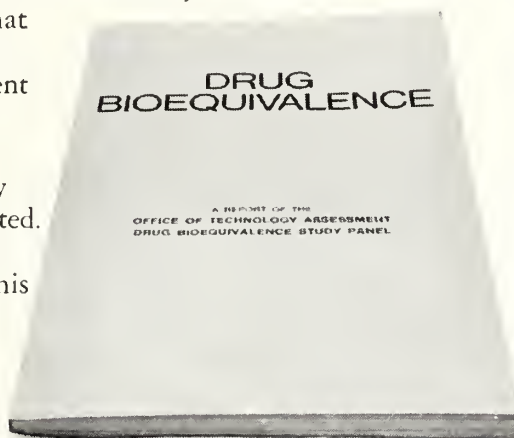
If the pharmacist substituted a chemically equivalent drug for the one you have specified for your patient—could you be certain of that product's safety and effectiveness simply because the chemical content was the same?

Definitely not, unless bioequivalence tests and other quality assurance checks had been conducted. The pharmaceutical industry and many scientists have maintained this position for years, but others have questioned it. Now the Office of Technology Assessment of the Congress of the United States has reported on the issue in its Drug Bioequivalence Study.*

Here are a few definitive statements in the O.T.A. report:

"...the problem of bioinequivalency in chemically equivalent products is a real one. Since the studies in which lack of bioequivalence was demonstrated involved marketed products that met current compendial standards, these documented instances constitute unequivocal evidence that neither the present standards for testing the finished product nor the specifications for materials, manufacturing process, and controls are adequate to ensure

that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.



"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and

(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or (c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...



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Washington, D.C. 20005

*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

protecting the integrity of your prescription

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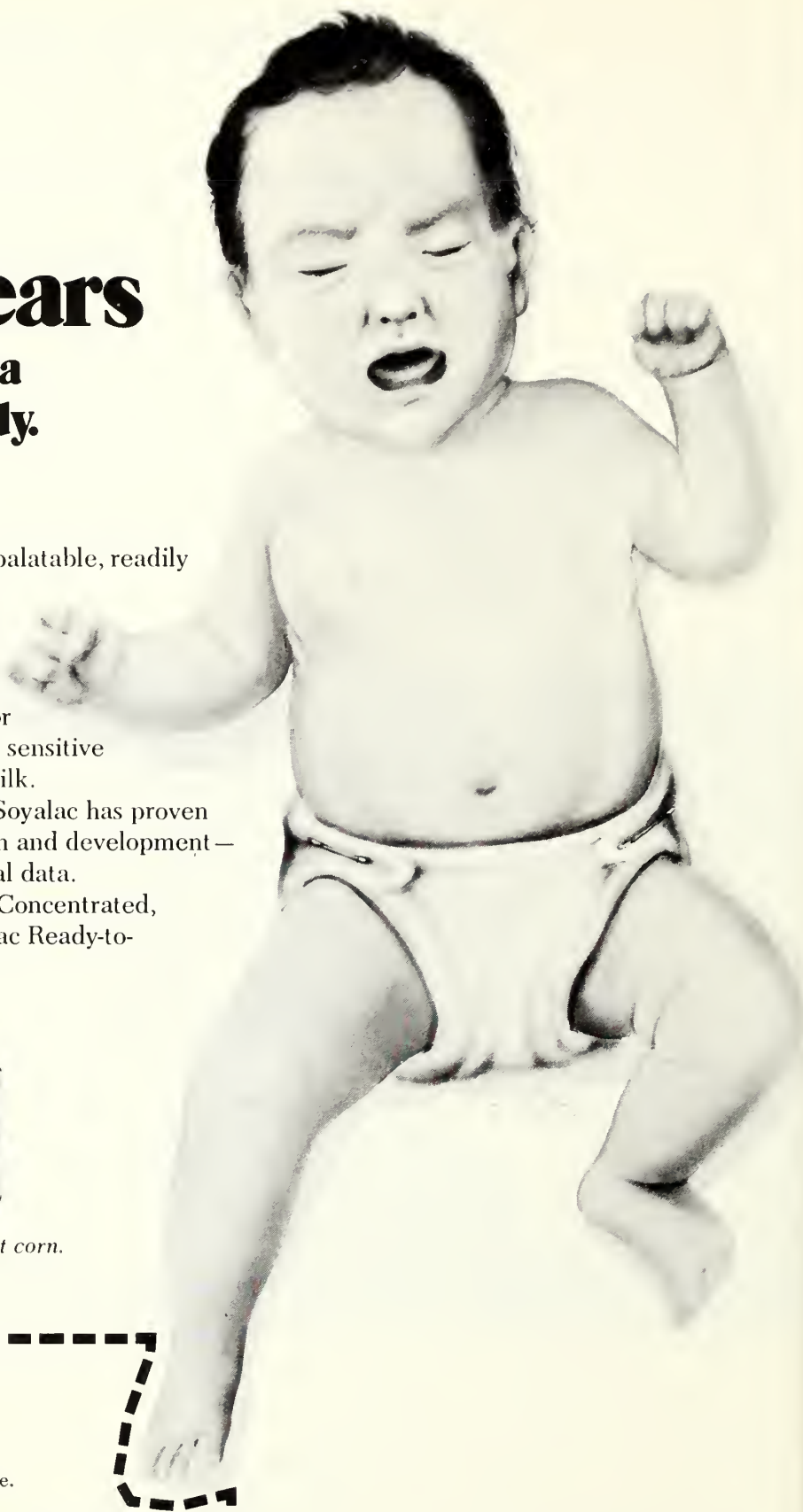
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NUMBER 6

PARACELSUS AND THE ORIGINS OF THE STUDY OF OCCUPATIONAL DISEASES*

JOHN P. DOLAN, Ph.D.**

Few figures in the history of medicine have stirred more controversy than has Phillipus Aureolus Theophrastus Bombast von Hohenheim, called Paracelsus. His proclivity towards verbosity and ostentation has made his middle name "Bombast" synonymous with pretentiousness in the languages of the West. Contemporaries referred to him as a medical Luther because of his violent attacks upon traditional Galenic medicine and his public burning of the *Canon of Avicenna* while professor at the University of Basel. His refusal to lecture in Latin and his contempt for many of his fellow physicians marked him as an unpopular innovator. Most of his contemporaries considered him an impostor and a fraud.

Yet in recent years he has, after four centuries, been rehabilitated and among many other accomplishments now attributed to him are that he was the founder of iatro-chemistry, the discoverer of vitamins, the first genuine psychologist, and the prototype of the Swiss Red Cross doctor. A growing interest in Paracelsus during recent decades has been due, to a large extent, to the exhaustive efforts of the German medical historian Karl Sudhoff who, between 1922 and 1933, pub-

lished some fourteen volumes of his works. Earlier in the century the eminent historian, Dr. Max Neuberger, wrote of him: "In bringing chemistry to a higher plane and making the new accessory branch useful to medicine, in comprehending the value of dietetics, in teaching the use of a great number of mineral substances, in paving the way for the scientific investigation of mineral water, in essentially improving pharmacy by the preparation of tinctures and alcoholic extracts . . . he has achieved really fundamental merit of all time."¹

Today, he is regarded not only as the true founder of iatro-chemistry, but also as the real pioneer in the treatment of mental diseases. The Swiss historian Josef Strebel considers him the precursor in the discovery of vitamins, anticipating the work of Leibig and Eijkman.² Philologists have acclaimed him for having played an important role in the development of modern European languages.³ Curiously enough, interest in the Swiss born physician has not been limited to his voluminous writings. He himself has been diagnosed. Basing their conclusions upon a portrait located in the Louvre and falsely attributed to Albrecht Durer, a number of physicians have suggested because of the goiter-like appearance of his throat that

*This article is from a forthcoming book, "Documentary History of Medicine," by W. N. Adam Smith and J. P. Dolan.

**Departments of History and Public Health, University of South Carolina, Columbia, S. C.

he suffered from an endocrine disorder. His birth and childhood in the Alpine region would seem to justify this conclusion. His notorious antifeminism is attributed to the fact that he was accidentally castrated at the age of thirteen by a wild boar. This fact was first brought to public attention by one of his adversaries at the University of Heidelberg, Thomas Erastus,⁴ and was given serious consideration by the famous "Dutch Hippocrates," Herman Boerhaave.⁵

Paracelsus, as he called himself after the famous Roman medical historian Celsus, was born in Einsiedeln, Switzerland, in 1493, son of a prominent local physician. The family moved to Villach in Carinthia when Theophrastus was ten years of age. Here his father was appointed physician for the famous School of Mining maintained by the Fugger Company. An early familiarity with mining and smelting was an important factor in Paracelsus' later studies on the subject of the diseases of miners and smelters.

Records of his medical education are somewhat obscure. After attending a number of German universities, he obtained a degree in medicine from the University of Ferrara in 1515. Thereafter he travelled extensively throughout Europe (1521-1525), spending some time in the military service of the Republic of Venice. In 1527 he was appointed city physician (Stadtarzt) and University Professor at the city of Basel. Here he included among his patients the great Humanist, Erasmus of Rotterdam, and the famous printer, Johann Froben.

One of his first moves as city physician was to suggest that all druggists be subjected to municipal supervision to insure the purity of their products and a reasonable price. He also immediately aroused criticism of his unorthodox methods of lecturing in German rather than Latin. His public burning of the *Canon of Avicenna*, one of the most highly regarded medical texts of the time, led eventually to his dismissal in 1528. Thereafter, he

led a wandering life writing and lecturing voluminously on theology, cosmology, alchemy, natural history and philosophy.

In recent years attention had focused upon Paracelsus' work, *Miner's Sickness (Von der Besucht und Anderen Bergkrankheiten)*, written in 1537 when he was employed in the Fugger mines of Villach, and published in 1576. The monograph is regarded by historians as being the first comprehensive study of industrial and occupational disease. The ancients were of course aware of occupational disease. Hippocrates describes a case of lead poisoning⁶ and Pliny wrote of the poisonous influence of lead, mercury and sulfur. The latter describes in his *Historia Naturalis* the masks worn by those who worked in the manufacture of cinnabar, or the red oxide of lead. "They protect the face with masks made of bladder skin, in order to avoid inhaling dust, which is extremely dangerous, the covering is sufficiently transparent to allow the person to see through."⁷

Paracelsus work consists of three books, each of which contains four tractates. In the first of these he treats the pulmonary diseases of miners, discussing successively etiology, pathogenesis, symptomatology and therapy. The second book treats diseases of smelter workers and metallurgists and the third deals with morbid conditions resulting from mercury poisoning.

Basic to all of Paracelsus' theories of disease is his belief that there are three invisible substances that form the physical body of man and that they are symbolized as sulfur, salt and mercury. The sulfur represents the auras and energies, the salt the material and substantial parts of the body, the mercury the fluids. In each organ these three substances are combined in certain proportions differing one from the other. Lung diseases, originating from the air which he calls chaos, are the result of these three basic elements settling in the lungs in three ways, in a mercurial manner like a smoke that condenses, like a salt vapor that solidifies and

like sulfur which congeals on the walls. Paracelsus is aware that poisons can enter through inhalation or as solids through the mouth, and that the poison is much weaker when inhaled, thus distinguishing between acute and chronic poisoning. He describes chronic arsenic poisoning with the well known symptoms of pallor, gastro intestinal disturbance and skin eruptions.

Although Paracelsus tends to mix Neo-Platonism and astral influences with his science, many of his observations have a modern and familiar ring. For example, he is well aware of the greater susceptibility of miners to other respiratory diseases, such as bronchitis, influenza, pneumonia and tuberculosis, which are found today to be more common among miners than in any other group.⁹

Paracelsus seems to be aware also of the fact that lung diseases are due to a variety of causes.¹⁰ It is the consensus of modern medicine that pneumoconiosis is a complex malady, "not a single disease process, but a composite of multiple disorders. These include (1) the primary dust molecule, (2) silicons, (3) chronic bronchitis and bronchiolitis, (4) centriobular, panlobular, and paracribrical emphysema, and (5) tuberculosis and occasionally other disease process."¹¹

The question of antigens is also raised by Paracelsus analogically as the notion of one element balancing another. Through the use of *aqua panis porcini*, or extract of cyclamen root, he advises that the lungs can be brought in to a diaphoretic condition so that nothing evil can be attached to them.¹² There is evidence in our time that would seem to indicate that bronchitis with its diaphoretic symptoms may itself protect against acute pneumoconiosis.¹³

The third book of *Miners Sickness*, in treating of mercury poisoning, also finds Paracelsus in advance of his time. Mercury, as with other minerals, has its positive and negative aspects; its proper balance must be observed. "Quicksilver contains within itself good and evil united in

such a way that they cannot be separated. As a result, whatever evil happens to you can be ascribed to both the good and the evil, but whatever good happens must be ascribed to both of them together."¹⁴

The signs of mercurial poisoning recorded by Paracelsus evidence first hand observation — gastronomical disorders tremor, oral putrefaction, cachexia, blackening of the teeth and increased salivation.¹⁵ He believes that the deposition of mercury takes place in a mechanical manner. "Every mercury settles in the cavities of the joints, that which passes through the backbone and hip region falls into the knee joints or ankle joints through corresponding ligaments."¹⁶

Therapy consists of creating an opening through which the mercury can flow out. This can be accomplished by applying a plaster for several weeks thus producing an ulcer "until the scab drops off by itself and the quicksilver runs out." The plaster is to be made of "realgris albi," alkali of lime and oil of roses. A further cure is the use of baths, specifically sulfur, either natural or artificial. He writes: "The dead mercury must be revived so that it can leave through this exit (i.e., through an ulcer). Here is how it is revived. First prepare a strong water bath of herbs rich in mucus, of the buds of firs or juniper bushes and also of fresh fir cones that have been boiled. Allow the patient to bathe in this as hot as he can, considering his strength. The same can be done in hot springs of Pfiffers, Baden, Plumbers, Gastem, Doeplitz, Asheke, or in artificial sulphur."¹⁷

Paracelsus was also familiar with what was termed *mala metallorum*, a fatal disease of the lungs which affected miners. In more recent years this has been found to be a form of cancer caused by the different carcinogenic agents such as iron, nickel, the chromates, asbestos and all types of radioactive materials.

In spite of his heavy reliance upon a belief in astral and cosmological influences, Paracelsus produced not only the

first comprehensive account of occupational disease, he also undertook to relate this to the overall body of medical knowledge and theory. Harold Fisch, writing in the *Cambridge Journal* says of him: "In fact Paracelsus may be said to have initiated the modern science of chemistry and medicine by substituting reliance on experiment for blind acceptance of authority."¹⁸ This sentiment is reiterated by the British medical historian Walter Pagel who writes: "Hence it is to Paracelsus . . . that we owe the new conception of disease in the establishment of three new doctrines, namely: (1) the external cause is the essence of the disease, (2) the organ involved and the anatomical changes de-

cide the nature of the disease, and (3) disease consists of a complicated disturbance of organ metabolism which secondarily reflects on the whole system."¹⁹

Paracelsus died in Salzburg, Austria, on the 24th of September, 1541, at the age of 48. He was buried in the church of St. Sebastian where his remains are to be found to this day. The epitaph over his grave reads: "Here is buried Phillip Theophrastus, distinguished Doctor of Medicine who with marvellous art cured dire wounds, leprosy, gout, dropsy and other incurable diseases of the body and who gave to the poor for distribution the goods he accumulated."²⁰

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6. Hippocrates: Epidemia, VI, 25.
7. "Qui minum in officinis poliuunt, faciem laxis vesicis inligant, ne in respirando perniciousum pulverem trahant et tamen super illas spectant," Plinii Naturalis Historia, Lib. xxxiii, LX. 122.
8. "Aus dem Sulphur wachst der Corpus, das ist der ganze Leib ist ein Sulphur, und es sind der Sulphura viel; das Blut ist ein andere Sulphur, das Fleisch ein anderer usw. Nun ist weiter die Kongelation, die Festkeit, des Corpus aus dem Salz; . . . Also ist nun das dritte der Mercurius, derselbige ist der Liquor"—Opus Paramirum, Lib. I, Cap. IX, 82.
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14. "und also ist das Quecksilber in ihm selbst, dass es Gut und Bos miteinander vereinigt hat, also dass sie nit von einander zu scheiden sind. Aus der Ursach folgt, was Boses dir gescheit, dasselbige ist dem Gutem und dem Bosen beiden anaulegen, und was Gutes geschieht, is aber ihnen beiden anaumessen." Von der Bergsucht.
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FIBEROPTIC COLONOSCOPY

LOUIS F. KNOEPP, JR., M.D.*

The fiberoptic colonoscope is essentially a long flexible sigmoidoscope, capable of being introduced through the anus to the ileocecal valve. It depends on two fiberoptic bundles, each containing 150,000-200,000 glass fibers about 10 micra in diameter and coated with a uniform layer of glass resin of a different refractive index from that of the main fiber. Light falling on one end is bounced along the inner core off the walls of the fiber, emerging at the other end with 95% of its original intensity.¹ One fiber bundle carries the light illumination from an ordinary movie projector lamp down the colonoscope into the interior of the colon. Another fiber bundle carries the image seen at the end of the instrument back to the eye. The image is focused by lenses at either end. There are two additional channels through the colonoscope: one transmits air for distention or water for irrigation, and the other serves as a conduit for the passage of biopsy forceps, a wire snare, or a fulgurating electrode. The instrument is 165 cm. long (ACMI) or 187 cm. long (Olympus). This compares with the standard rigid sigmoidoscope of 25 cm.

Through a colonoscope it is possible to visualize suspicious lesions seen on barium enema, find polyps too small to be seen on barium enema, biopsy, photograph, and remove pedunculated lesions with the snare. Small lesions can be fulgurated.

The fiberoptic endoscope was developed at the University of Michigan between 1954-1958.² In Japan in 1957 gastrocameras and sigmoidocameras were developed. Colonoscopy really came to the

fore in 1969 when Shinya and Wolff began to popularize it and remove polyps through it.³

This paper reports our experience with the 165 cm. ACMI colonoscope (Figure 1).

MATERIALS AND METHODS

From December 1972 to April 1975, 123 patients underwent 127 colonoscopies at either the Mary Black Memorial Hospital or the Spartanburg General Hospital.

Usually the patients received a clear liquid diet the day prior to the examination, and a cathartic, usually two ounces of castor oil, the evening before, and tap water enemas until clear the morning of the examination.

The patient is placed on the examining table in the left Sims or the supine position. Either local anesthesia or general anesthesia was used. Most patients received local anesthesia which is desirable. Usually intravenous narcotics have to be given for supplementation. All colonoscopies were done in the operating room. Fluoroscopy was not available. If there was difficulty passing the colonoscope, portable abdominal films were taken as needed. If there was still difficulty, the examination was stopped.

The colonoscope is introduced through the anus under direct vision. The rectosigmoid is immediately visualized by instilling air and irrigating with water as needed. The colonoscope is advanced by direct vision into the sigmoid colon to the descending sigmoid junction. Here it is helpful to use the alpha maneuver (counter clockwise rotation as described by Sakai).⁴ It is helpful to have an assistant who advances the instrument as the op-

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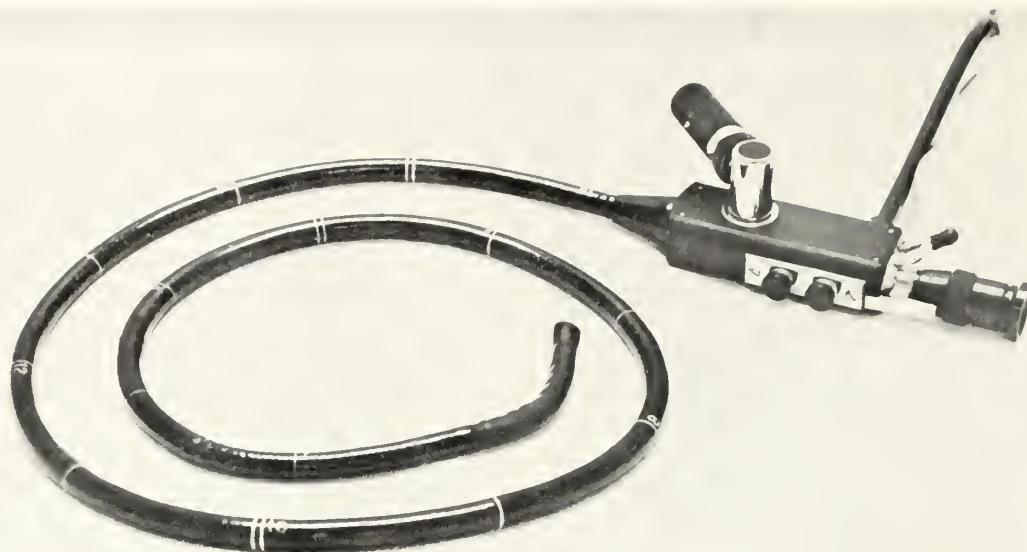


FIG. 1
The 165 mm. ACMI colonoscope

erator directs the tip with the four way controls. Usually when the tip passes the splenic flexure the alpha loop must be straightened out by clockwise rotation before one can proceed through the transverse colon. The position of the colonoscope can best be determined by x-ray or fluoroscopy, but with experience an examiner can tell where it is by the light shining through the abdominal wall, or by certain landmarks in the colon, such as the ileocecal valve (Figure 2).

Polyps were removed with the ACMI Bovie and the ACMI Wappler Endoscopy snare, using room air.

The success of this procedure highly depends on good analgesia, a good bowel prep, and the skill and patience of the examiner. Success improves with experience.

RESULTS

The distance examined in 127 colonoscopies is depicted in figure 3. The three inadequate examinations were due to poor preparation, angulation from carcinoma, and angulation from diverticulitis. An examination was terminated when either the pathology was reached or when it be-

came too painful, took too long, or excessive angulation of the colon was found. The cecum was reached in 4 of the first 50 examinations (8%), 9 of the second 50 examinations (18%), and in 9 of the last 27 examinations (33%).



FIG. 2
The colonoscope inserted to the cecum

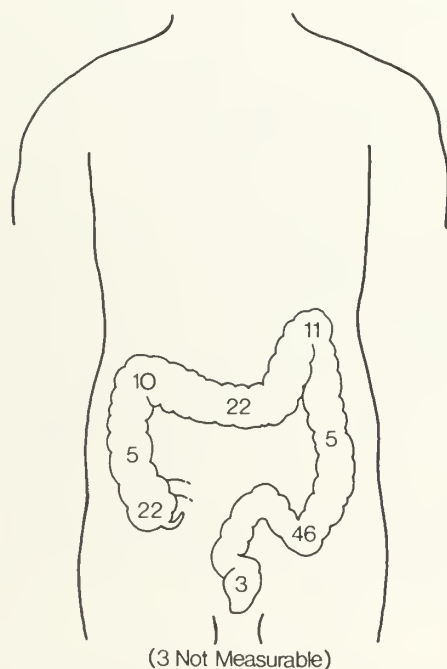
FIBEROPTIC COLONOSCOPY

Indications for colonoscopy included questionable barium enema lesions, carcinoma, polyps, undiagnosed rectal bleeding, polyps found on sigmoidoscopy (to look for others), anemia, history of colon cancer, ulcerative colitis, Crohns disease and pseudomembranous colitis.

The most frequent indication was to evaluate a barium enema lesion. Colonoscopy was most helpful in distinguishing diverticular strictures from carcinoma, and in evaluating questionable polyps. Eighty percent of the time the lesion in question could be reached.

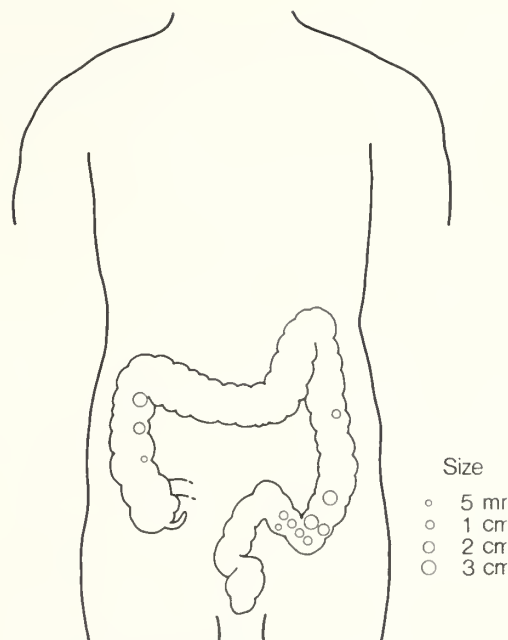
The second most common indication was undiagnosed rectal bleeding. Three of thirty-seven patients were found to have lesions causing bleeding by the colonoscope. Carcinoma was found in one, a large polyp in another, and three large polyps in a third. None of these lesions was reported on the barium enema.

One patient presented with obstruction of the colon at the descending sigmoid



Distance Examined in 127
Colonoscopies

FIGURE 3



12 Polyps Snared By Colonoscopy
(In 10 Patients)

FIGURE 4

junction, apparently from volvulus. This lesion was found on barium enema and reduced by colonoscopy.

Many polyps were found on colonoscopy, missed on barium enema. If they were less than 5 mm in diameter they were sometimes biopsied but usually left alone. (The size can be estimated by comparing the polyp with the open jaws of the biopsy forceps—7 mm across.)

Polyps greater than 1 cm were removed by sigmoidoscope snare if possible or by colonoscopic snare if above the sigmoidoscopic level (Figure 4). Two sessile polyps were removed by partial colon resection, and one probable pedunculated polyp in the descending colon could not be reached by the colonoscope. Of the 12 polyps snared, 11 were adenomas and 1 was juvenile polyp.

No complications occurred in this series.

CASE REPORTS

MC, a 69-year-old white female, was seen in the office with irregular bowel habits, bright and dark rectal bleeding and protruding hemor-

FIBEROPTIC COLONOSCOPY

rhoids. Sigmoidoscopy to 20 cm was normal. Barium enema was reported normal. Hemocult through the sigmoidoscope was positive. Review of the barium enema revealed a questionable lesion. The patient was given an anesthetic for a hemorrhoidectomy, and while asleep a repeat sigmoidoscopy and colonoscopy were done. An obvious carcinoma was found at 35 cm. Several days later a sigmoidectomy was done without complications. Pathology revealed a Dukes B adenocarcinoma.

I.G., a 75-year-old white male, was seen for bleeding hemorrhoids. Sigmoidoscopy revealed minimal internal hemorrhoids but a bleeding polyp at 10 cm. Colon x-ray done twice showed diverticulosis only. Colonoscopy to the lower descending colon revealed 3 pedunculated polyps, all 15 x 15 mm, at 25, 30, and 35 centimeters. These 3 polyps were removed by colonoscopic snare, and the lower polyp was removed by sigmoidoscopic snare. All were adenomas. The patient had no problems and no further bleeding.

DISCUSSION

Colonoscopy is probably the greatest single advance in the diagnosis and management of colonic disease made in this decade. Its obvious advantage lies in its ability to clearly distinguish questionable intraluminal lesions seen on colon x-ray film without resorting to a laparotomy. It is useful for removing polyps above the reach of the proctoscope. It is much more accurate than a colon x-ray in identifying early polyps or carcinomas of the colon. It has been used during laparotomy to localize polyps in the colon and to search for additional polyps; in such cases one surgeon opens the abdomen and another handles the colonoscope from below.⁵ It has been used at laparotomy to localize teliangectasias of the small intestine.⁶ It is used to look for second lesions in patients with one carcinoma or polyp. It has been utilized to delineate mucosal inflammatory disease above the range of the proctoscope. It can be used to follow patients who have had a previous colon resection

for carcinoma.

Who should be colonoscoped? Opinions range from everyone over forty to only those with polyps seen on colon x-ray film. The answer should be in between. Every patient should have an adequate barium enema and proctoscopy first. Suspicious lesions on barium enema are a strong indication. A good argument for doing a colonoscopy on everyone with undiagnosed rectal bleeding can be made. Diarrhea in selected patients may be an indication. All polyps above the sigmoidoscopic range should be removed colonoscopically if possible.

There are several disadvantages to colonoscopy. It can be very difficult to do an adequate examination; particularly if one is learning how. The examination may be very slow. It is somewhat painful. The equipment is expensive and easily broken. There is a hazard of perforation of the bowel, or hemorrhage, especially when fulgurating. Wolff and Shinya have recommended that a physician not attempt snare colonoscopic polypectomy unless considerable experience has been gained with diagnostic colonoscopy.³

CONCLUSION

Fiberoptic colonoscopy is a significant advance in diagnosis and management of diseases of the colon. Its indications are not clearly delineated. Its use should be restricted to those physicians who can spend enough time to develop the necessary expertise. It should be done on patients with questionable lesions on barium enema and on those with undiagnosed rectal bleeding. After one has developed experience, it is the procedure of choice for removal of polyps above the reach of the rigid sigmoidoscope.

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“DOCTOR CAESAR” AND HIS CURE FOR POISONS AND RATTLE-SNAKE BITES

BUFORD S. CHAPPELL, M.D.*

Friday morning, November 24, 1749, in the South Carolina Commons House of Assembly:

“A Member acquainted the House that he had been credibly informed a Negro Man named Amory, now belonging to Mr. Joseph Stanyarne of John’s Island had been put on board of a Ship on the Coast of Guinea, with design to have him sent to England for Education; but the Master of the said Ship had treacherously sold the said Negro as a Slave in this Province, to one William McLurer, late of John’s Island, deceased. And then he moved the House to give Directions therein for the Relief of said Negro.

“And another Member acquainted the House that there is a Negro Man named Caesar belonging to Mr. John Norman of Beach Hill who has cured several of the Inhabitants of this Province who had been poisoned by Snakes. And that he had been informed that the said Negro Man Caesar was willing to make a Discovery of the Remedy which he makes use of in such Cases for a reasonable Reward.

“Resolved that a Committee be appointed to enquire into the Circumstances of the said Negro Amory. And also to consider the services done by the said Negro called Caesar. And to report the same, as it seems to them, with their Opinion thereupon, to the House. And also to consider of and report what Reward the said Negro Caesar shall merit for his Services.

“And a Committee was appointed accordingly of the following Gentlemen,

*Columbia, S. C.

that is to say, Doctor Dale, Doctor John Rutledge, Captain Taylor, Mr. Mathews, Mr. Dart, Major Boone, Mr. Irving, Mr. Mazyck, and Mr. Austin.

“Ordered that it be an Instruction to the said Committee that they have Power to desire the Aid and Observations of any skilful Physicians that they shall think fit in relation to the Discoveries and Services of the said Negro Man named Caesar.”

In the afternoon session of the Commons House, Friday, November 24, 1749, the committee appointed to study the cases of the Negro men, Amory and Caesar, was ordered to sit. A second sitting was ordered for the afternoon of Tuesday, November 28, 1749.

On Wednesday morning, November 29, 1749, Dr. Glenn and Dr. Bisbane was added to the committee. “And Mr. Austin reported, from the said Committee that they had, pursuant to the Order of the House, examined into the Services lately done by the Negro Man called Caesar and also considered what Reward the said Caesar may merit for his Services, and had directed him to report the same, as it appears to them, to the House, and he read the Report in his Place, and afterwards delivered it in at the Clerk’s Table, where the same was read to the House, and is as followeth, that is to say,

“The Committee who were appointed to enquire into the Circumstances of a Negro Man named Amory, now belonging to Mr. Joseph Stanyarne of John’s Island, also to examine into the Services lately done by a Negro Man called Caesar, be-

longing to Mr. John Norman of Beach Hill, and to whom it was given in charge to desire the Aid and Observations of any skilful Physicians they should think fit, in relation to the Discoveries and Services of the said Negro Caesar and to report what Reward they should be of the Opinion that the said Negro may merit, report,

"That having called Mr. William Miles before the Committee and examined him, as to what Services had been done by the said Caesar in his Family, he informed the Committee he verily believed his sister had been poisoned, and was cured by Caesar; and that some Time afterward his Brother seemed affected with a very odd Disorder, and, suspecting that it was the Effects of Poison, sent for Caesar who relieved him instantly. And that the said Mr. Miles suspects his Son to be in the same Situation, and wants Caesar to his Relief.

"Henry Middleton, Esq., being examined, seem to believe his Disorder proceeded from Poison, as he found a good Effect from the first Dose of Caesar's Antidote, and after the second Dose the Symptoms of his Disorder intirely left him. He also informed the Committee that his Overseer apparently was in a worse Situation than himself, and has been intirely relieved by the same Hand.

"Mr. John Norman (Caesar's Master) was next examined, who informed the Committee that, to his Knowledge, Caesar had done many Services in a physical Way, and in particular had frequently cured the Bite of Rattle Snakes, and never knew him to fail in any one Attempt. That Caesar had been called upon as a Doctor in many Cases by the Neighbors, and mentioned an Instance to the Committee of a Negro Man who had been cured of the Yaws by Caesar when he had twice been salivated, and was covered with an entire Scab from Tip to Toe. And another Point Caesar is very famous in is the Cure of Pleurisies many of which he had undertaken to the Knowledge of Mr. Nor-

man which have had very deadly Symptoms.

"Mr. Sacheverell informed the Committee that Caesar had undertaken to cure a Man who was violently afflicted with Fits, and, in Appearance, will affect it.

"And then the Committee called the said Negro Caesar before them, and asked him on what Conditions he would discover his Antidotes, and such other useful Simples as he was acquainted with, who answered that he expected his Freedom, and a moderate Competence for Life, which he hoped the Committee would be of the Opinion deserved one hundred Pounds Currency per Annum. And he proposed to give the Committee any satisfactory Experiment of his Ability they please as soon as he should be able to provide himself with the necessary Ingredients.

"The Committee therefore recommended that upon his satisfactory Discovery of his Antidote against Poison, he shall have his Freedom, and an annual Allowance of one hundred Pounds for Life with such a further Allowance for any other useful Discovery he may make to the Public as this House shall think fit.

"The last Paragraph of the said Report, being read a second Time, was agreed to by the House.

"Resolved that two Persons to be nominated by this House and two other Persons to be nominated by the said John Norman (Caesar's Master), if he shall be so content, do appraise the said Negro Caesar, and if the Persons so nominated cannot agree, then they do choose a fifth Person, whose Judgment shall be final as to the Value of the said Negro.

"And the House being informed that the said Mr. Norman attended at the Door, he was called in, and the Speaker (by Order of the House) acquainted him with the said Resolution, and then asked him if he was willing to agree to it, and he answered that he was content. And then he withdrew.

"Resolved that this House will make

Provision for the Payment to the said John Norman for the appraised Value of the said Negro Caesar.

"Resolved that this House will make a farther Provision for the said Negro Caesar, for any further Discovery he shall make of any useful Medicine.

"Ordered that the said Negro Caesar do attend this House, and that the Speaker do acquaint him with the said Resolutions, and direct him to reveal to the said Committee all the Secrets he knows in Physic, as well as Antidotes against poison as any other.

"And the House being informed that the said Negro Caesar attended at the Door, he was called in, and Mr. Speaker acquainted him with the said Resolutions and Order. And then he withdrew."

Thursday Morning, December 7, 1749.

"Mr. Mathewes reported to the House that Mr. Singellton and himself (pursuant to their Order) met with Mr. Thomas Bullen and Mr. Richard Bedon, the two Persons nominated on behalf of Mr. John Norman, the Proprietor of the Negro Man Caesar, to appraise the said Negro Caesar. But the said Persons, not agreeing upon the Value of the said Negro, had chosen Thomas Lamboll, Esq., to be the Umpire, pursuant to the Resolution of this House for that Purpose, who had returned an Appraisement of the said Negro upon Oath, which he presented to the House, and the same was received and read, and is as followeth, that is to say,

The 7th day of December, 1749

"Thomas Lamboll, nominated (and sworn) Umpire by Mr. Richard Bedon, Mr. Thomas Bullin, Mr. Richard Singellton, and Anthony Mathewes, Esq., Arbitrators to declare the Value of a certain Negro Man Slave named Caesar of Mr. John Norman's, between his said Master and the Public, which hath treated him for the freeing of the said Slave, upon hearing his said Master and each of the said Arbitrators upon that Subject, doth finally adjudge upon due Consideration of all the Advantages of the said Negro

Slave Caesar (aged near sixty seven Years) might be of to the Owner by his Knowledge and Skill (as represented to him) may be worth the Sum of five hundred Pounds Current Money of South Carolina, and at that, and no more, he is valued by

Thomas Lamboll, Umpire."

A resolution was made and the Commons House ordered the payment of the five hundred pounds, current money of South Carolina.

Friday Afternoon, March 16, 1750, the committee made its report,

"That the Committee have, pursuant to the Order of the House, examined into the Cures performed by the Negro Caesar and the Efficacy of his Antidote for expelling the Poison, and it appeared to the Committee that the said Caesar hath cured several Persons who had been long ill of a lingering Distemper, attended with intolerable Pains in the Stomach and Bowels, particularly Mr. John Cattell, Mr. Henry Middleton, and Mr. Gaillard, who had employed some of the most skilful Physicians in the Country, and found no Relief from their Medicines. But the Committee finding the said Negro Caesar dangerously ill of a Fever, had no opportunity of making Trial of any Experiments upon Animals; but they insisted upon his discovering everything he knew concerning the Cure for Poisons, together with the Names of the Plants which he had made Use of in performing the aforesaid Cures, and his Method of preparing and administering the same, as likewise the Symptoms by which he knew when any Person was poisoned, which he said he would faithfully comply with and accordingly declared as follows, to wit,

THE CURE FOR POISON

"Take the Roots of the Plantane and wild Hoare-hound, fresh or dried, three ounces; boil them together in two Quarts of Water to one Quart, and strain it; of this Decotion let the Patient take one third Part three Mornings, fasting successively, from which if he finds any

Relief, it must be continued until he is perfectly recovered. On the Contrary, if he finds no Alteration after the third Dose, it is a sign that the Patient has not been poisoned at all, or it has been with such Poison as Caesar's Antidotes will not remedy, so may leave off the Decotion. During the Cure the Patient must live on a spare Diet, and abstain from eating Mutton, Pork, Butter or any other fat or oily Food.

"N.B. The Plantane or Hoar Hound will, either of them, cure alone, but they are most efficacious together.

"In Summer you may take one Handful of the Roots or Branches of each in Place of the three ounces of the Roots of each.

"For Drink during the Cure, let them take the following,

"Take the Roots of the Golden Rod, six Ounces, or in Summer two large Handfuls of the Roots and Branches together, and boil them in two Quarts of Water to one Quart (to which may be added a little Hoare Hound and Sassafras); to this Decotion, after it is strained, add a Glass of Rum or Brandy and sweeten it with Sugar for ordinary Drink.

"Sometimes an inward Fever attends such as are poisoned for which he orders the following,

"Take a Pint of Wood Ashes and three Pints of Water; stir and mix them well together; let them stand all Night, and strain or decant the Lye of(f) in the Morning of which ten ounces may be taken six Mornings following, warmed or cold, according to the Weather. These Medicines have no sensible Operation, though sometimes they work in the Bowels, and give a gentle Stool.

"The Symptoms attending such as are poisoned are as follows,

"A Pain of the Breast, Difficulty of breathing, a Load at the Pit of the Stomach, an irregular Pulse, burning and violent Pains of the Viscera above and below the Navel, very restless at Night, sometimes wandering Pains over the whole Body, a Reaching and Inclination

to vomit, profuse Sweats (which prove always serviceable), slimy Stools both when costive and loose, the Face of a pale and yellow Colour, sometimes a Pain and Inflammation of the Throat; the Appetite is generally weak, and some cannot eat any; those who have been long poisoned are generally very feeble and weak in their Limbs, sometimes spit a great Deal; the whole Skin peals, and likewise the Hair fall off.

"CAESAR'S CURE FOR THE BITE OF A RATTLE SNAKE

"Take of the Roots of Plantane or Hoare Hound (in Summer Roots and Branches together) a sufficient Quantity; bruise them in a Mortar, and squeeze out the Juice, of which give, as soon as possible, one large Spoonful; if he is swelled you must force it down his Throat. This generally will cure, but, if the Patient finds not Relief in an Hour after, you may give another Spoonful which never fails.

"If the Roots are dried, they must be moistened with a little Water.

"To the Wound may be applied a Leaf of good Tobacco moistened with Rum.

"Ordered that the said Report be printed, and that the said Committee do direct the same to be done."

"Doctor Caesar," of St. Paul's Parish, "Practioner of Phisick" made a will but the date of its making and the date of his death is not known. The will was recorded on May 17, 1754, and he probably died a short time before this date. Benjamin Chappell and Joshua Clark were witnesses to the will and James Baker and Andrew Way were named executors. He desired that all of his estate be turned into money and that his wife, Lily, a slave of Captain John Norman, be given ten pounds; and that his daughter, Lucy, be given twenty pounds. All the rest of his estate to go toward the purchase of his daughter Hannah's freedom or supply any of her needs. If she is freed, she is to have the rest of his estate when she reaches eighteen years of age. Should she die before her freedom, the rest of his estate to go to his grand-

DOCTOR CAESAR

children, Peggy and Caesar.

Some two years later on June 8, 1756, Captain John Norman made his will which was proven on November 11, 1757. Captain Norman must have died in the Fall of 1757. Several slaves were mentioned in his will but it was to his daughter, Sarah Norman, that he left a "mustizo"

girl named Hannah.

Did Hannah ever gain her freedom? I don't know. Many years later, toward the end of that century, there died in Charleston a woman of some little property and by the name of Hannah Ceazer who left her estate to be administered by her friend, Jacob Cohen.

REFERENCES

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Pages 293, 294, 302-304, 326, 478-480.

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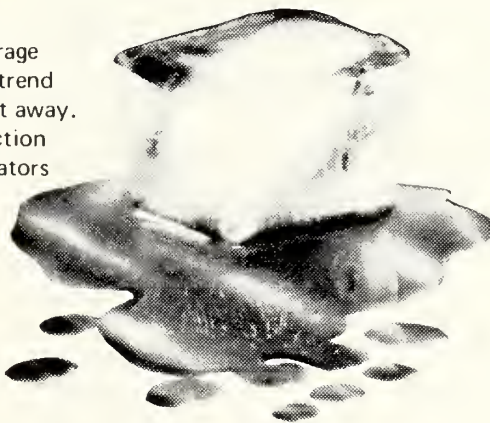
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BRUCE MAYNE, EMINENT SCIENTIST DOCTOR OF PUBLIC HEALTH

B.S.A. M.Sc. D.P.H. H.C. T.M. London
Imperial Malariologist, Government of India
Special Expert, U. S. Public Health Service

WILLIAM S. HALL, M.D.*

South Carolina, and especially South Carolina State Hospital, is more than just a footnote in the pages of dramatic medical research because of the renowned Dr. Bruce Mayne—British-Born, a world traveler of recognized depth and experience, an eminent scientist who commanded international respect, an expert photographer with artistic sensitivity which matched his research-oriented mind—whose ashes now are encased in a simple urn in Elmwood Cemetery.

While his life spanned but 58 years, Dr. Mayne greatly extended the horizons of knowledge for the benefit of mankind.

Internationally recognized and acclaimed as an outstanding scientist, particularly in the field of malariology, Dr. Mayne played a vital role in the colorful history of the South Carolina State Hospital in Columbia in 1931 until he passed away in 1941.

The preparation of his biography posed a real challenge, necessitating inquiries far and near. Contacted were friends, acquaintances, and attorneys in Columbia; co-workers in the U.S. Public Health Services located in Washington, Atlanta, and Panama; U.S. Government Agencies in Washington; Fort Bragg at Fayetteville, N. C.; the U.S. Bureau of Naturalization in Columbia and Charleston, S. C., as well as two universities in California.

Dr. Mayne was a brilliant conversation-

alist, especially referable to world events and the intriguing globe-wide places he had visited. There was always an eagerness to discuss scientific experiences and his hobbies, particularly photography, his collection of far Eastern objects of art, and fascinating dolls of foreign lands.

As the result of his lifelong pursuit of photography, Dr. Mayne contributed valuable photos of parasites and insects, many being reproduced in standard textbooks.

As a member of the Columbia Camera Club, he often gave illustrated travel talks, filled with delightful and gorgeous colored slides of unique and beautiful areas, especially in the Orient. Treasured photographs of the famous Taj Mahal are now in several Columbia homes. His photos were on display in libraries and the Columbia Museum of Art. In the book, "The Red Carolinians" by Chapman J. Milling, M.D., former medical staff member of S. C. State Hospital, are splendid ones of Catawba Chief Blue, other Indians, and artifacts.

A man of scholarly achievements, broadened by extensive travel, as well as by the association with the friendship of distinguished scientists and other persons of importance in all parts of the world, Dr. Mayne was unusually reticent about his personal life and background. He was really an enigma. There was friendliness to a certain level, generosity in many ways, always a willingness to share interesting experiences and to discuss his intriguing scientific work, but never any

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mention of personal life or family.

Dr. Mayne's early life and family history are shrouded in all the elements of a mystery; however, a few facts have been ascertained. There is even the intriguing fact of a name change. From the United States Bureau of Naturalization in Columbia and Charleston, S. C., information was secured that he was born in Middlesex, England, on September 29, 1882, with the name of Maurice Bruin Mitzmaine. Nothing could be learned about his parents nor with whom he came to the United States through the Port of New York in 1884.

There is no information as to where he went from New York, but—and here is an element of drama—as Maurice Bruin Mitzmaine, he was admitted to the University of California at Berkeley in January 1903 as a special student in the Undergraduate Division, College of Agriculture. The degree of Bachelor of Science was conferred May 13, 1908. While attending the University, he was one of the first students of Professor William B. Herms under whose influence his groundwork in medical entomology was laid.

Again he entered the University of California at Berkeley in September 1908, with the degree of Master of Science (Agriculture) conferred May 17, 1910. His Master's thesis was "General Observations on the Bionomics of the Rodent and the Human Fleas."

During his University years, many scientific articles, most of them referable to insects and fleas, were written for publication in the *Entomological News*; the *Canadian Entomologist*; *Parasitology*; and *Public Health Bulletins*. Even before leaving the University of California, he began to contribute to the field of medical entomology by his association with the study of the San Francisco plague epidemic.

There must be a drama behind the questions which remain unanswered to this day. When did Dr. Maurice Mitzmaine become Dr. Bruce Mayne? and, the linger-

ing question, why?

In the Philippine Islands, apparently between 1911-1915, many articles referable to activities under the name of Dr. Bruce Mayne were published in the following Scientific Journals: *The Philippine Agricultural Review*, *American Journal of Tropical Diseases*, and *Public Health Reports*. As reported in the *Philippine Journal of Science*, 1913, Vol. 8, Sec. B., pp 223-229, Dr. Mayne helped to clear up the puzzle of the transmission of surra by showing that it could be transmitted by *Tabanus striatus*.

Before and after his work in the Philippines, Dr. Mayne was associated with the U.S. Public Health Service, where he became interested in the role of insects in the transmission of malaria. While working in this field he helped to clarify the question of American anopheline hosts for malaria. One of the most interesting results was the evidence he found demonstrating that man was the winter carrier of malaria organisms instead of the hibernating mosquito. During the 28-year period in which Dr. Mayne served in the U.S. Public Health Service, he was associated with various aspects of diseases transmitted by insects.

The Hunger Fighters by Paul De Kruif, of Readers Digest fame, author of *Microbe Hunters* (1928), contains accounts of courageous, imaginative men, scientists, who by tedious, lengthy research contributed tremendously for mankind in the battle against hunger. These include the fight to find the wheat that would survive the worse weather in the United States; development of serum for hog cholera; the eradication of foot and mouth disease in cattle and deer; and the discovery by the "Automatic Man," Edward Francis, of the new disease to which he gave the musical name of Tularemia. For a brief period of time, Dr. Mayne worked with Dr. Francis on this research.

Some time was spent by Dr. Mayne in the Southern part of the United States with a malaria survey among 7,500 school

children in a rural section of Georgia, according to the Georgia State Board of Health reports of 1925. There also was a report of a survey to determine malaria prevalence in the Okefenokee Swamp in Georgia. In 1925 he received from the University of Georgia the degree of Doctor of Public Health.

Dr. Mayne, a citizen of Great Britain, already well established and recognized as an eminent malariologist, was, from 1926 to 1929, in India for the malaria survey for the Imperial Government of India. Upon returning to the United States, his activities were resumed with the U.S. Public Health Service on a "loan basis" from the British Government.

As previously stated, the year 1931 was especially significant in the history of the South Carolina State Hospital. In that year, the Office of Malaria Investigations, National Institute of Health, U.S. Public Health Service, under the direction of Dr. L. L. Williams, Jr., of Washington, D. C., reached the decision to establish a field station for the purpose of perfecting methods of the use of malaria in the treatment of neurosyphilis, of studying the biology of malaria, and the distribution of materials.

Dr. Bruce Mayne was assigned to the selection of the proposed field station. This selection was to be made on the basis of certain advantages available to the service, namely, centralization in geographic position to the hospitals purported to be served, from Boston, Massachusetts, to Detroit, Michigan, on the North, and from the Louisiana border to the Georgia seaboard on the South.

Many locations were visited and carefully considered for the proposed station. Dr. Mayne chose the South Carolina State Hospital in Columbia, and, after a trial period of four months, so much dependence was placed on the work at S. C. State Hospital that it was designated the National Headquarters, beginning November 1, 1931.

Upon Dr. Mayne's recommendation, the

U.S. Public Health Service surrendered the plan of combining a Southern location with a Northern one (New York or Washington) for the full conduct of a Service Headquarters, and agreed to make the S. C. State Hospital in Columbia the Centralized National Station for the United States in the distribution of material for malaria therapy. Dr. Mayne assumed the position of Director on November 1, 1931, and occupied this position until he passed away April 30, 1941.

In his progress report of November 1931, Dr. Mayne stated that the decision to select the S. C. State Hospital was in no small measure prompted by the wholehearted interest and accord of the Hospital Superintendent, Dr. C. Fred Williams, and the intelligent, sympathetic cooperation of the clinical director, Dr. E. L. Horger, as well as the entire staff of the Hospital. Progress was rapid and continuous with favorable results of inoculated patients in the S. C. State Hospital.

During the first year, mosquitoes infected from S. C. State Hospital patients were transported for malaria therapy to state hospitals in Raleigh and Morganton, N. C.; Milledgeville, Georgia; Bolivar, Tenn.; and Torrance, Penn.; Gallinger, St. Elizabeth's and Walter Reed Hospitals in Washington, D. C.; the U.S. Army Medical School in Washington; U.S. Naval Hospitals in Philadelphia; and on League Island, Penn.; U. S. Veterans Hospitals in Augusta, Georgia, and in Excelsior Springs, Missouri. The distribution of information and materials rapidly extended throughout the United States and soon became worldwide.

There were two distinctive contributions, under the direction of Dr. Mayne, to the progress of malaria therapy of general paresis in the United States:

1. A strain of *Plasmodium Malariae* (Quartan Malaria) was established in 1931, and studied continuously for its biology and its use as a therapeutic agent. This was the first instance recorded in any country. It constituted one of the most

reliable sources for therapeutic malaria, and was widely used in mental hospitals throughout the United States up until the time Penicillin was discovered.

The quartan strain was established through efforts of the Columbia Station from the natural case obtained from the town of Dubach, Louisiana, through the courtesy of Dr. T. B. H. Anderson, Medical Officer in Charge, U.S. Marine Hospital, at New Orleans, La. Centers were inaugurated in Tallahassee, Florida, Baltimore, Maryland and in Columbia, S. C.

2. Dr. Mayne's second distinctive contribution was the preparation of serum derived from dissected malaria infected mosquitoes to produce the infection in paretics.

Requests for materials were received in addition to the regions mentioned, from Western United States, from the British Ministry of Health in London, from Czechoslovakia, and other distant parts.

Dr. Mayne and his staff successfully started what was popularly referred to as the mosquito farm, offering a stock of insect carriers for uninterrupted work in the transmission of malaria throughout the United States. The original material for this mosquito farm was gathered from areas as remote as Texas and Florida. Stocking the insectary from material collected locally would have been indeed difficult because of the scarcity of anopheline mosquitoes in this section of South Carolina. Continuous stocking of this insectary was of great importance because of the general absence of material during the dormant winter period.

In the course of the work with malaria, two new remedies were tested, plasmochin and atabrine. With the first, the staff demonstrated that this drug not only cured malaria in patients after a few courses of treatment, but it also rendered the patient's blood non-infectious for mosquitoes for long periods. This was of an effective prophylactic against community infection.

With atabrine, a new malaria remedy

was demonstrated for the United States, giving promise of tremendous economy in the treatment of this disease by inducing a cure after only five days of administration.

The remarkable achievements of Dr. Mayne and his staff at the Malaria Laboratories gained more and more international recognition which naturally brought more recognition to the South Carolina State Hospital. Seeking knowledge from the laboratory, there were visits of eminent scientists from the United States, from Spain, Asia, England, various European countries, and China. Cooperation was afforded the American Society of Syphilologists by providing a large quantity of material from malaria cases for their use in studies referable to the standardization of the Wassermann reaction.

Dr. Mayne was in popular demand for seminars, lectures, and demonstrations at annual meetings of the Southern Medical Association, the American Psychiatric Association, the S. C. Academy of Science, the Science Club at Winthrop College, Rock Hill, S. C., and many others. Educational activities with exhibits were presented at the American Public Health meeting in Pasadena, California; the Western State Hospital, Fort Steilacoom, State of Washington; and the University of California Medical College. He held symposia for the North Carolina District Medical Society, the Orangeburg, S. C. Medical Society, Columbia Medical Society, LeConte Scientific Society in Columbia; medical students and laboratory technicians from the University of South Carolina; the S. C. Baptist Hospital Nurses Alumnae; S. C. State Hospital Nurses Alumnae; the medical staff, graduate nurses and student nurses at the S. C. State Hospital, and many other groups.

In recognition of his outstanding work in medical entomology, in 1935, he was designated as an official representative of the U. S. Public Health Service to the

International Congress of Entomology in Madrid, Spain. In 1938 he was the delegate to the Third International Congress of Tropical Medicine and Malaria in Amsterdam, Holland.

He was associate editor of several scientific journals devoted to malaria and tropical medicine, including the "Revista di Malariologia," and was the author of more than 75 papers on scientific subjects.

Associated with Dr. Mayne during his tenure and ably assisting him at the Malaria Research Laboratories was Dr. Martin D. Young, zoologist, who succeeded Dr. Mayne as Director upon the latter's death. In fact, Dr. Young also became internationally recognized in malariology in his own right. Other staff associates included the following: Dr. G. Robert Coatney, protozoologist; Wallace P. Greenwood, medical technician; Hans E. Hingst, senior medical technician; E. V. Welch, junior entomologist; David F. James, scientific assistant, Trawick H. Stubbs, scientific assistant; and Mrs. E. Greenwood.

In 1933, Dr. Mayne's activities were interrupted to work with Doctors L. L. Williams, Jr. and J. P. Leak in the St. Louis encephalitis epidemic. These scientists tested the theory of encephalitis transmission by mosquitoes on themselves, on convicts, and on mice, but found no evidence that mosquitoes were the vectors.

In October 1939, work at the laboratories in Columbia was again interrupted by the departure of Dr. Mayne for China and Burma. He had been appointed by the U.S. Surgeon General as Technical Advisor to the Malaria Commission to assist the Chinese Government in the investigation and control of a serious malaria epidemic in Southwest China and along the well-known Burma Road.

The Malaria Commission to China returned with a highly gratifying report of their cooperative investigations. They succeeded in establishing hospitals and laboratories for the control of the malaria

outbreak, as well as training a large number of medical officers and recent medical graduates in fighting the menacing malaria situation.

For his services Dr. Mayne received the personal acknowledgement of Generalissimo Chiang Kaishek.

Early in January 1940, Dr. Mayne began feeling bad and losing weight. Upon arriving in Rangoon, Burma, he became incapacitated because of severe abdominal pains. Colonel Morrison (I.M.S.), in whose care he had been placed, tentatively diagnosed the condition as early peptic ulcer. This he shortly changed to malignancy of the stomach. Dr. Mayne wished to return to the United States for surgery, and was flown from Rangoon by Clipper Plane to the U.S. Marine Hospital in Baltimore, Maryland. An operation revealed well advanced cancer of the stomach.

Dr. Mayne passed away in Baltimore on April 30, 1941, and in compliance with his personal directions, was cremated and the ashes sent to Elmwood Cemetery in Columbia, South Carolina.

Research into the life of this amazing research crusader revealed yet another puzzle, equally as intriguing as his change of names. Over the years there had been no knowledge or any indications that Dr. Mayne was, or ever had been, married. Yet, upon his death and at the final rites for this world-recognized scientist, there was a surprise mourner—a daughter. She was Miss Ruth Mayne, associated with the U.S. Army Laboratory at Fort Bragg, Fayetteville, N. C.

Attorney R. Beverly Herbert of Columbia, with whom Miss Mayne had conferred, called her lonely plight to the attention of Dr. and Mrs. Chapman J. Milling who at once invited her to be their guest on the S. C. State Hospital campus.

Miss Mayne was astonishingly like her father in appearance, mannerisms and scientific interests although they had not been together since she was a small child. His career had been followed through the

BRUCE MAYNE

years and she had acquired many of his articles and books. While charming and appreciative of the courtesies of the Milling family and others, she was as reticent as Dr. Mayne concerning personal and family affairs. It was only from official records that it has been learned that on June 15, 1909, in Oakland, California, Dr. Mayne married a lady "Marion," whose surname is illegible on the available documents. It was also learned they were separated in 1922.

Nothing has been known of Miss Mayne since sometime after the settlement of Dr. Mayne's affairs; and Attorney Herbert has advised that his last information several years ago was that she and her mother were in New Orleans. No address could be secured, nor whether Miss Mayne had married.

Dr. Mayne became a member of the Episcopal Church while in India; and on January 17, 1940, while in Rangoon, codicils were added to his original will prepared in Columbia, S. C., on January 1, 1939.

He was possessed of Postal and United States bonds and had accounts in several South Carolina banks; in the Chase National Bank in New York; with Lloyd's in London, as well as in the Imperial Bank

in India.

Dr. Mayne had a sense of humor which must be added as a footnote. He delighted in teasing Dr. Catherine N. Munro, the S. C. State Hospital woman physician. She could never remember his birth date. So, he frequently changed this, and she always responded with a nice gift which he graciously accepted.

There is no monument to Dr. Bruce Mayne, just a simple marker in Elmwood Cemetery, Columbia, where the cremation urn was placed. He did not request a monument, for surely there was full knowledge of the transience of things that men carve out of stone.

His monument is the gratitude of the thousands of victims of general paresis whose improvement, or recovery, from that heretofore fatal illness resulted from his exhaustive studies and activities and his success in developing the serum from malaria mosquitoes. In addition, there is the gratitude from the thousands of malaria victims world-wide who were cured as a result of his research and expertise in malariology.

Dr. Mayne was literally fascinated and devoted to his chosen life's work—and he gave it his life.

Medical University of South Carolina

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Measuring cause and effect

Cause: High levels of anxiety

Effect: Exacerbation of irritable bowel syndrome



When barium fills the whole colon, there is also a reflux through the ileum so that ileum is superimposed on colonic shadows. The tube-type descending colon revealed is normally associated with the diarrheal phase of the irritable bowel syndrome.

Case History:* 27-year-old female

Before treatment

Chief Complaint: Abdominal pain and diarrhea.

Present Illness: Intermittent, left-sided, lower abdominal pain for over a year; pain, unassociated with menstrual periods or eating, lasted several hours. Abdominal symptoms occurred in attacks lasting 1-2 days with remissions of 3-4 days. Diarrhea accompanied attacks. No weight loss, nausea or vomiting.

Personal History: Married, 2 children. Somewhat restless, tense and anxious.

Physical Examination: 8/16/73. System review within normal limits. Weight 95 lbs. Petite, pleasant, cooperative patient with no obvious signs of illness.

Abdomen: Spastic, tender sigmoid colon. Otherwise normal.

Rectal: Normal mucosa and stool. No rectal bleeding or excess mucus or fat in stools.

Sigmoidoscopy: Normal sigmoid mucosa.

Laboratory tests: Within normal range. No occult blood in 3 successive stool examinations.

Impression: Irritable bowel syndrome. X-rays 7/25/73 showed tube-type descending colon. Librax, one capsule *q.i.d.*, prescribed as adjunctive therapy on 8/23/73. Symptoms of anxiety evaluated with Hamilton Anxiety Scale on same date.

*Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley, N.J. 07110.

Although this is an actual case history, not all cases of irritable bowel syndrome can be expected to respond this rapidly to therapy.

Before Evaluation				
0	1	2	3	
0	1	2	3	
0	1	2	3	
0	1	2	3	
0	1	2	3	
0	1	2	3	
0	1	2	3	
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0	1	2	3	
0	1	2	3	
0	1	2	3	
0	1	2	3	
0	1	2	3	
0	1	2	3	
Pretreatment				
Total Score				
Anxiety				
Somatized Anxiety				

Undue anxiety—often a forerunner of irritable bowel syndrome

Irritable colon is a disorder commonly seen in the average physician's daily practice. Expressed as diarrhea and/or constipation, the disorder affects mainly the colon's tonicity. Usually spasms are produced, mediated through the autonomic nervous system. Such abnormal activity can easily derive from emotional stress, which causes parasympathetic stimulation. Hence the direct relationship between anxiety and irritable bowel syndrome. Reducing anxiety, one

of the causative factors, can be expected to counter the effect, exacerbation of irritable bowel syndrome.

Librax is the logical adjunct in treating irritable bowel syndrome

☐ Dual action of Librax helps relieve both anxiety and somatic symptoms.

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Relief of symptoms linked to relief of anxiety

After treatment

Abdominal pain and discomfort less troublesome although still some frequency and looseness of the bowels. Patient felt significantly better and less anxious. Bowel movements returned to regular pattern when therapy discontinued on 10/4/73.

10/4/73: Second Hamilton Anxiety Scale completed. **Follow-up** (2 months later): Patient off all therapy, normal bowel function, no abdominal pain, no significant anxiety feelings or undue tension or nervousness.

Hamilton Anxiety Scale	
Parameters	After Evaluation
Anxious Mood	0 1 2 3 4
Tension	0 1 2 3 4
Fears	0 1 2 3 4
Intellectual	0 1 2 3 4
Depressed Mood	0 1 2 3 4
Insomnia	0 1 2 3 4
Somatic (muscular)	0 1 2 3 4
Somatic (sensory)	0 1 2 3 4
Cardiovascular Symptoms	0 1 2 3 4
Respiratory Symptoms	0 1 2 3 4
G.I. Symptoms	0 1 2 3 4
G.U. Symptoms	0 1 2 3 4
Autonomic Symptoms	0 1 2 3 4
Behavior at Interview	0 1 2 3 4
Patient's first evaluation was made 8/23/73 prior to treatment. The second evaluation, made 10/4/73, shows concurrent drop in anxiety and somatized symptoms.	Posttreatment Total Score 4 Anxiety 1 Somatized Anxiety 3

Charted at left, the Hamilton Anxiety Scale ratings show how somatized anxiety symptoms—especially gastrointestinal, the complaint rated highest—diminished along with anxiety symptoms. The first six parameters plus "behavior at interview" measure anxiety and the remaining seven, somatized anxiety. Between the first and second evaluations, the sum of the anxiety and the sum of the somatized symptoms each decreased by 4 points on the rating scale.

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**for the anxiety-related symptoms
of irritable bowel syndrome**

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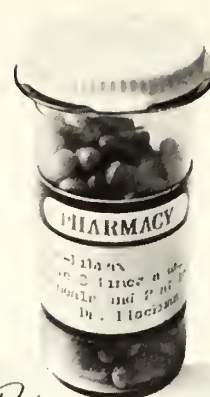
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and 2.5 mg clidinium Br.



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and T i.h.s.*

Initial R_x

The initial prescription permits evaluation
of patient response to therapy



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and T i.h.s.*

Follow-up

Follow-up therapy with a prescription for
2 to 3 weeks' medication usually helps
maintain patient gains.

for the anxiety-related symptoms of irritable bowel syndrome • duodenal ulcer • upper functional gastrointestinal disorders

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Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depres-

sion; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

Dosage: Individualize for maximum beneficial effects. Usual maintenance dose is 1 or 2 capsules, 3 or 4 times a day, before meals and at bedtime. Geriatric patients—see Precautions.

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President's Page



Dear Fellow Physicians of South Carolina:

It is a great privilege for me to have the opportunity of serving you as your President for 1975/76. The activities since the Convention at Myrtle Beach have really been rapid and fast-moving.


The major thrust since the Convention has been in the medical liability insurance problem. We have undergone several telephone conference calls with the Liability Committee and with the members of the Executive Committee and the entire Council of the South Carolina Medical Association. There have been three meetings with the State Insurance Commissioner culminating in a public hearing on Tuesday, May 27.

On Thursday, May 29, 1975, the State Insurance Commission declared a crisis and has activated the Joint Underwriters Association. In my opinion this has been the most responsible and responsive approach to the problem of malpractice and it is the best solution for the patients and for the physicians and hospitals in South Carolina at the present time. As you know, this will be a temporary solution. the joint underwriting will expire on December 31, 1977. Meanwhile, a committee has been authorized by the Legislature to study the problem and come up with long range recommendations for the 1976 session of the Legislature. There will be doctors representing the Medical Association on that committee and we are maintaining close contact with the members of the Legislature to effect necessary changes in the laws.

The present Joint Underwriters Association will furnish claims-occurrence type insurance on a pool basis of all the liability carriers in the State, representing over 100 insurance companies. These premiums will be higher than our previous premiums and will be somewhat in line with the proposed claims-made rates as proposed by St. Paul Insurance Co. This Underwriters Association will operate on a non-profit basis, and if there are excess monies in the fund these will be returned to the insured in the form of smaller premiums the following year or a rebate. If there is a shortage it will be necessary to assess the insured doctors to make up the deficit. I believe that this is the most fair and equitable method at the present time to approach the malpractice problem until the permanent solution can be found.

There are many other activities that we are going forward with at the present time, but these will follow in later news reports. Again, I wish to express to all of our members my appreciation for the opportunity to serve as your President.

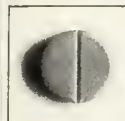
C. Tucker Weston, M. D.,
President

A black and white photograph of three children in a dilapidated wooden structure, possibly a house under construction or a shanty town. One child is sitting on a wooden ledge in the foreground, looking directly at the camera. Another child is leaning out of a window in the background, looking to the side. A third child is standing on a higher level of the structure, looking down. The scene is gritty and evocative, suggesting a need for health care in impoverished areas.

**Ortho announces
a unique,
broad-spectrum
anthelmintic
effective against
whipworm...**

new
Vermox TRADEMARK chewable
(mebendazole) tablets

...and highly effective against roundworm, hookworm and pinworm in single or mixed infections



No dosage calculations — one simplified dosage,
regardless of weight or age†

whipworm, roundworm, hookworm and mixed infections:

1 chewable tablet b.i.d. for 3 consecutive days

pinworm: 1 chewable tablet

If the patient is not cured three weeks after treatment, a second course of treatment is advised.

highly effective

	Mean cure rates	Mean egg reduction
Whipworm	68%	93%
Roundworm	98%	99.7%
Hookworm	96%	99.9%
Pinworm	95%	— — —

simplicity of administration

patients can take the tablet at any time.
It can be chewed, swallowed or crushed and mixed with food. No messy liquids to pour.

not a dye new Vermox* (mebendazole) chewable tablets will not stain clothes, teeth, feces, toilet bowls, etc.

convenient neither laxatives nor special diet required. Therapy does not interfere with daily activities.

well tolerated

transient symptoms of abdominal pain and diarrhea have occurred
in cases of massive infection and expulsion of worms.

Vermox has not been extensively studied in children under 2 years of age, and thus, the relative benefit/risk should be considered before treating these children. Vermox is contraindicated in pregnant women. (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Indications Vermox* (mebendazole) is indicated for the treatment of *Trichuris trichiura* (whipworm), *Enterobius vermicularis* (pinworm), *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed infections.

Efficacy varies in function of such factors as pre-existing diarrhea and gastrointestinal transit time, degree of infection and helminth strains. Efficacy rates derived from various studies are shown in the table below:

	Trichuris	Ascaris	Hookworm	Pinworm
cure rates mean (range)	68% (61-75%)	98% (91-100%)	96% —	95% (90-100%)
egg reduction mean (range)	93% (70-99%)	99.7% (99.5-100%)	99.9% —	— —

Contraindications Vermox is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

*TRADEMARK

Precautions **PREGNANCY:** Vermox has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since Vermox may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and administration The same dosage schedule applies to children and adults.

For control of trichuriasis, ascariasis, and hookworm infection, one tablet of Vermox is administered morning and evening on three consecutive days. For control of enterobiasis, a single tablet of Vermox is given.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

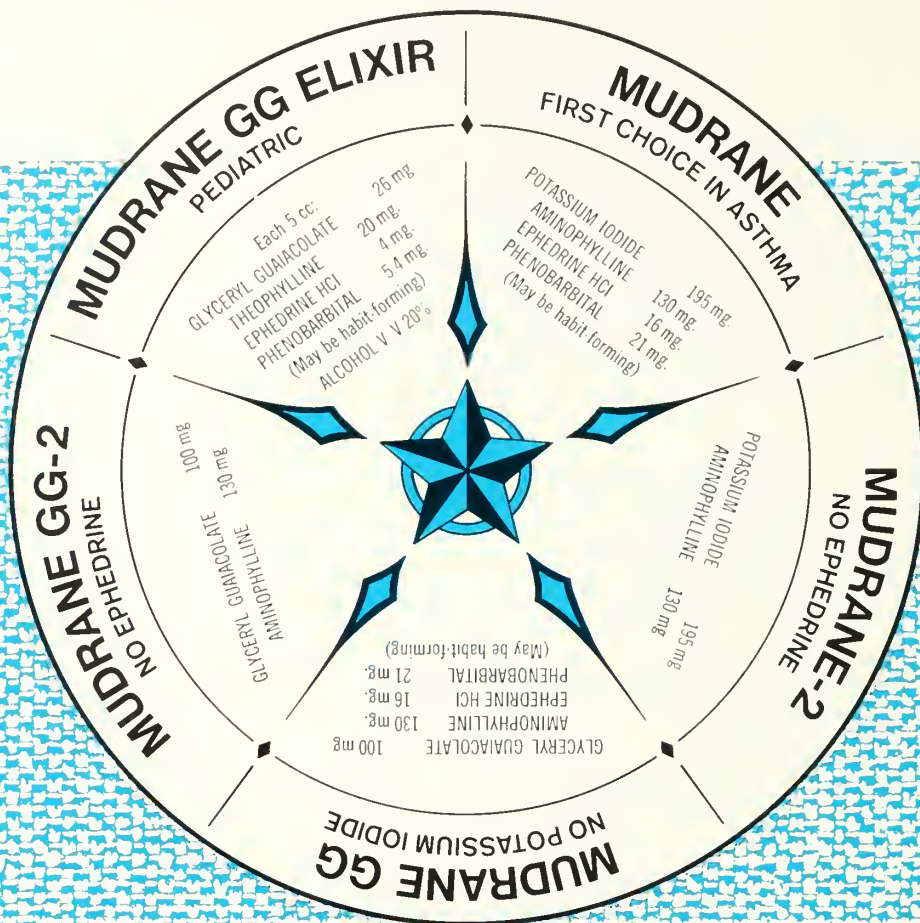
How supplied Vermox is available as tablets, each containing 100 mg of mebendazole, and is supplied in boxes of twelve tablets.

Ortho Pharmaceutical Corporation,
Raritan, New Jersey 08869



The MUDRANES

Discreet formulations of four well regarded drugs for the relief of bronchial distress—Potassium Iodide, Glyceryl Guaiacolate, Aminophylline, Ephedrine with Phenobarbital (to lessen cardiac stimulation).



INDICATIONS: For the prompt symptomatic relief of bronchial asthma, emphysema and bronchiectasis. The Mudranes dilate the bronchi and liquefy mucus plugs. **DOSAGE:** Tablet; One tablet with a full glass of water 3 or 4 times daily as required. Divide tablet for child's dose. Elixir; Children, 1 cc for each 10 lbs. of body weight. May be repeated 3 or 4 times a day. Adult, one tablespoonful 4 times daily. All doses should be followed with a glass of water.

CONTRAINDICATIONS: Aminophylline/Theophylline is contraindicated in the presence of severe cardiac arrhythmias and patients with massive myocardial damage. Ephedrine, in presence of severe heart disease, extreme hypertension, and in hyperthyroidism. Phenobarbital, in porphyria and in patients with known phenobarbital sensitivity. Potassium Iodide, in pregnancy (to protect the fetus against possible iodine-induced depression of thyroid activity), in tuberculosis (produces gumma dissolution), and in acne; also in the presence of known iodide sensitivity. **PRECAUTIONS:** Aminophylline/Theophylline should be avoided in patients with massive myocardial damage and/or severe cardiac

arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdose. Potassium Iodide; Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing anginal pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdose. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

HOW SUPPLIED: Mudrane and Mudrane GG available in bottles of 100 and 1000 tablets; Mudrane-2 and Mudrane GG-2 in 100s; Elixir in pints and half-gallons.

Federal law prohibits dispensing without prescription.



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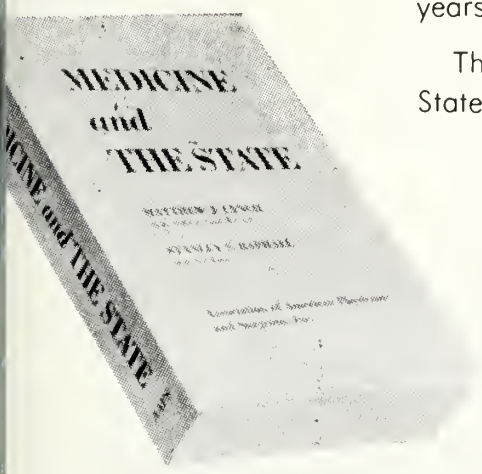


THE ASSOCIATION OF AMERICAN PHYSICIANS AND SURGEONS is a free, independent, non-governmental, voluntary organization of members of the medical profession. We are united for the purpose of analyzing the profession's problems and formulating actions to improve medical care for all Americans, preserve freedom of choice for patient and doctor, protect the practice of private medicine, and educate physicians and the public to recognize and resist schemes that would weaken or destroy our free-choice system of medical care.

The Association, founded in 1943 is nationwide with membership in all 50 states, Puerto Rico and the District of Columbia. It is nonpartisan, nonsectarian and nonsecret in character.

THE MEMBERS ARE DEDICATED TO: The ethics of the Physicians' Oath of Hippocrates to which medical doctors have bound themselves for over 2,000 years; and

The principles of individual liberty, to which the founders of the United States of America pledged their lives, fortunes and sacred honor.



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Editorials

Required Reading List

The following are *required* reading this issue:

1. Don Kilgore's Presidential Address.
2. Report of the Ad Hoc Committee on Long Range Planning.

Both of these powerful documents con-

tain so much truth and will have such a profound influence on the future practice of medicine in South Carolina that YOU must read them both!! Nuff said.

EEK

Fair Play and a Practical Realization

SCMA, through its intense activity and good judgment, has caused to be introduced into the State Legislature several separate pieces of legislation which will have a very beneficial effect for all citizens of South Carolina if enacted. I hope they are all law by the time you read this. Yet one of these acts, it seems to me, will force us to change our stance on a very fundamental issue.

One of the pieces of legislation introduced at the behest of the SCMA and staunchly advocated by the SCMA will set and limit fees charged by attorneys in medical liability cases. We are stating

that we approve of government setting professional fees. Henceforth, it seems to me, if we complain about the principle of government regulating our fees, we will be hypocritical, speaking out of both sides of our mouth, and advocating one thing for others and something else for us. Let us be aware of this and act accordingly. From now on, I might complain about regulated medical fees being unusual, uncommon, unreasonable, and too damn low, but I can nevermore complain about the fact of being regulated.

EEK

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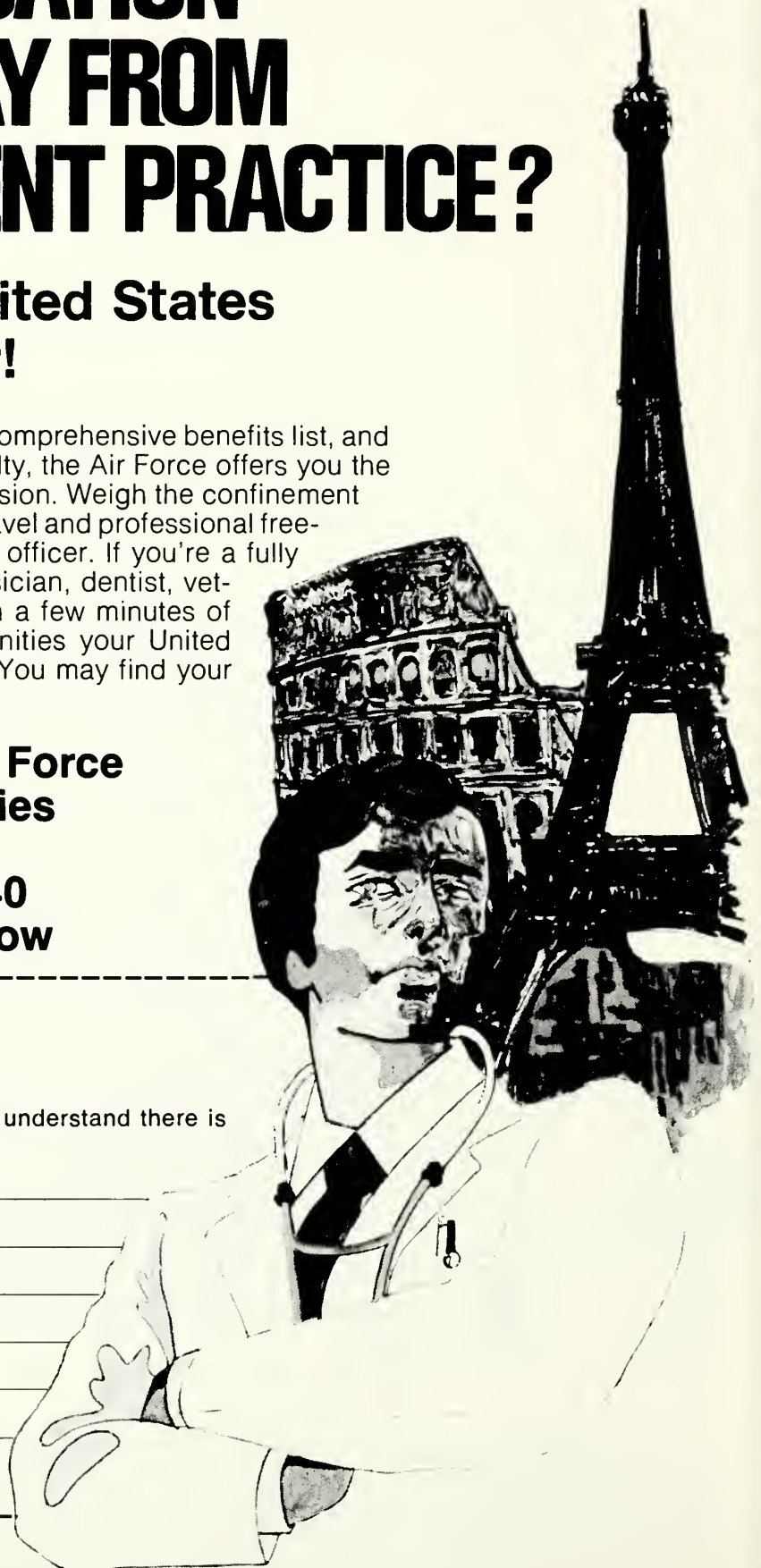
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Date of Birth _____

Air Force Medicine



**President's Address
South Carolina Medical Association
Monday, May 5, 1975**

Two years ago the members of the House of Delegates paid me the greatest honor of my life in choosing me as your President-Elect. At that time I told you that I appreciated the honor; but I realized that it also involved duties, responsibilities, and a lot of hard work. Today my term is almost over. I have tried to do my best and hope that I have lived up to your expectations of 1973. If I have accomplished anything, it has been only with the cooperation and help of the members of the S.C.M.A.

In some ways the power of the President of the South Carolina Medical Association is quite limited. The Executive Council runs the day to day affairs of the Association; and in this respect, the Chairman of the Council is a much more powerful figure than the President. At the annual meeting, the House of Delegates are led by the Speaker, who appoints the Reference Committees, and directs the work of the House. The Executive Director and his staff have the administrative authority for the day by day affairs of the Association. They are responsible for the lobbying; they make many of the contacts of the Association with the general public and special groups; and they watch over the financial well being of the Association. On the national level, your delegates and alternate delegates represent you at the AMA. Although the President may speak at Reference Committees with slightly more authority than the average AMA member, he certainly has no more rights. I believe this division of labor is entirely proper; because the Association is too big and complex for one man to attempt to lead all these activities.

After we eliminate all these activities, just what does the president do? 1) With the advice and consent of the Council, he appoints the chairmen and new members of all committees of the Association. The success or failure of the South Carolina Medical Association during that year, and partially for the next three years depends upon the wisdom of his choice. The President is an ex-officio member of all committees and should supervise their work as much as possible. 2) Secondly, the President is the representative of the Association. He is the spokesman for all of you with other professional groups, the legislature, Congress, the press, and the general public. The President should take advice and information from all members, but the ultimate responsibility for the success or failure of the policies and the stands of the Association belongs to the President. He needs to be well informed on all subjects related to the needs of the South Carolina Medical Association. It is an awesome

responsibility. 3) Part of the job of being well informed is to visit as many constituent medical societies as possible. This insures that the greatest possible number of members have contact with the President. On these visits, the President has the responsibility of informing all members present of the latest developments on the association level that affect the individual member. In turn, the president must be prepared to listen sympathetically to local problems, suggestions, and criticisms of the members. Unanswered questions should be referred to the Executive Director and the Executive Council for a mutual solution. 4) The President should be a leader. He should anticipate the needs of the Association, inform the members of these needs and be persuasive enough to get the members to work for the association and solve its problems. He should be a peacemaker and mediator if necessary. He should make sure that the South Carolina Medical Association provides the best possible service for its members. 5) Finally, the President must be a combination of information center and "Dear Abby" for the lay public. He must constantly insure the best public image for the South Carolina Medical Association.

During the past year, the one question I have constantly asked myself is, "What will be best for the members of the South Carolina Medical Association?" I have made mistakes in the past year. I have made people angry. But I hope that everyone will understand that whatever I did was with the good of the Association in mind; and I hope that they will forgive and understand. Very rarely, Fabian inactivity may be the best policy. Most of the time, however, quick decisive action is needed, and errors are often committed. But this should not make us afraid to act. Many years ago Theodore Roosevelt received a letter from a friend criticizing an appointee of Roosevelt's who was trying to do a good job under difficult circumstances. This critic previously had been offered a chance at the same job himself by Roosevelt and had turned down the position. Roosevelt pointed this out to him in very forceful words: "It is not the critic that counts, not the man that points out **how** the strong man stumbled, or **where** the doer of deeds could have done them better. The credit belongs to the man who is actually in the arena, whose face is marred by dust and sweat and blood; who strives valiantly; who errs, and comes short again and again because there is no effort without error and shortcoming; but who does actually strive to do the deed; who knows the great enthusiasms, the great devotions; who spends himself in a worthy

cause; who at the best, knows in the end the triumph of high achievement; and who at worst, if he fails, at least fails while daring greatly, so that his place shall never be with those cold and timid souls who know neither victory nor defeat."

This past year has been an extremely busy one. To mention all the important events that have occurred since last May would be impossible. As one of my professors once remarked, "What the mind can absorb is limited by what the seat can endure." Therefore I will concentrate on two problems, manifesting themselves this past year, which I believe are of the most critical importance to the medical profession.

The most obvious choice is the professional liability problem. Last summer the one major liability insurance carrier in South Carolina asked for a 72% increase in its premiums. Your Executive Council felt that this increase was probably justified, but we asked to see a loss record for South Carolina. This was refused very curtly and rudely by the insurance carrier. Because they represented the only carrier of importance in South Carolina, and because other carriers had announced their intention to terminate coverage in South Carolina, we did not strenuously oppose these increases when they were requested of the Insurance Commissioner. However, we did realize the importance of obtaining legislation in South Carolina for a climate that would attract other carriers to South Carolina and prevent rates from skyrocketing as they have in other parts of the country. From all that I can determine, South Carolina still has the lowest professional liability premiums in the United States, and we intend to keep them that way by all means within our power. Numerous meetings were held with legislators, insurance officials, government officials, and other interested parties in an effort to determine what legislative changes would be most helpful in preventing the professional liability situation from reaching a crisis point in South Carolina. Almost all of these people indicated that changes in the insurance laws and changes in the system for awarding damages would be desirable. Almost without exception, they also pointed out that before legislation of this type could be considered seriously, medicine should make proposals of its own which would assure the legislature and the general public that we are making every possible effort to be certain that all physicians in this state were practicing in an ethical and proper manner.

At the suggestion of the state insurance commissioner, a bill was introduced providing for a Joint Underwriting Association in South Carolina as a first step. Although this is a security blanket in case all else fails, no one really likes it. The insurance companies despise it. All doc-

tors who use it, will find it is hideously expensive. In summary, the Joint Underwriting Association resembles the old assigned risk driver's pool which we had in South Carolina a few years ago. Certainly *nobody* was fighting to join that! The most important disadvantage of the Joint Underwriting Association is that it does not attack the basic problems of the crisis. In many ways, it is like defleaing the dog, without cleaning out the doghouse. However, it does offer a last ditch security blanket. This bill has passed both House and Senate and now awaits the Governor's signature. A companion bill to this would set up a study commission consisting of lawyers, doctors, insurance representatives, legislators, and members of the general public to investigate the problems of malpractice in South Carolina over the next two years. The South Carolina Medical Association stands ready and willing to cooperate to the fullest in this study.

However, because a genuine crisis exists, we are pressing forward with legislation in which we believe will create a more rational climate for professional liability insurance in this state, without depriving the injured patient his rights or compensation. Because our problems are not unique, I have been working for several months in contact with the South Carolina Bar Association, the South Carolina Trial Lawyers Association, the South Carolina Claimants Attorneys, the South Carolina Hospital Association, the South Carolina Insurance Agents, the dentists, the accountants, the professional engineers, and the architects. Although many of these professionals are not in the crisis situation we are, their time is approaching rapidly. I understand that in my home city of Greenville, there are five suits pending against architects at the present time, and interestingly enough two of these have been brought by physicians. Legislation is urgently needed because, according to the recent massive study on malpractice by HEW, only 16¢ out of every dollar spent for professional liability premiums ends up as direct benefits to patients who suffer medical injuries. All the rest of it goes for plaintiff and defense lawyers, for the costs of investigation, for medical witnesses, for insurance underwriting costs, and for salesmen's commissions. The cost of such a system is outrageously extravagant and clearly wasteful. It is in sorry contrast with workman's compensation, where 73¢ out of every premium dollar goes to the injured patient.

In order to promote a system that protects the public without gouging, a system that recognizes legitimate medical injury, a system that takes care of those who are injured without unusual delay, and a system that compensates the patient according to the seriousness of his injury, the South Carolina Medical Association is intro-

ducing eight bills to meet this serious problem. Briefly summarized, these would: 1) Establish a ceiling on damages on a reasonable basis as in Indiana. 2) Shorten our unreasonably long statute of limitations. 3) Establish a fair sliding scale for contingency fees such as exists in New Jersey. 4) Eliminate duplication of medical costs already paid for by Medicare, Medicaid, and other third parties. 5) Limit awards for pain and suffering and punitive damages. 6) Eliminate windfall recoveries by establishment of reversionary trusts. 7) Eliminate the *Ad Damnum* clause, and 8) establish a state mediation system for small claims similar to legislation passed in New York.

This then is the status of professional liability insurance in South Carolina. Who bears the responsibility for seeing that a just and equitable system is set up? I say the responsibility lies with those who are directly involved: physicians, lawyers, insurance companies, legislators, and the general public. Let us examine each of the responsibilities. First the general public is responsible and should be vitally interested because it is paying heavily for exaggerated professional liability insurance costs and not even realizing it. I have already mentioned that only 16% of the professional liability premium dollar goes to the injured party. Juries are giving lavish awards. A heroin addict in jail attempted suicide

by jumping from a building and fractured his neck. He became quadriplegic and collected, not sued, for \$725,000 by alleging negligence by the prison physician in not preventing his suicide attempt (AMA News, March 3, 1975).

But the public pays in many other ways. Recent opinion surveys report that 50 to 70% of physicians polled said that they engaged in various forms of defensive medicine. It is estimated that millions of dollars each year are spent on unnecessary x-rays, unnecessary laboratory tests, unnecessary hospitalization, and unnecessary doctors bills. He pays in accentuation of the physician shortage. Dr. Malcolm Todd has pointed out each patient in the Long Beach Memorial Hospital pays \$3.65 a day to cover the cost of professional liability premiums contrasted to 10¢ a day 10 years ago. But the general public pays in a far more serious manner because when physicians fear liability, medical practice is reduced to a cookbook approach. Forced compliance with one method of treatment caused the stagnation of Babylonian and Egyptian medicine. Almost all progress, and certainly all revolutionary progress is going to be achieved by going against the prevailing concepts of the times. History has many examples of this: Copernicus, Galileo, Newton, Einstein, and in the medical field Ambrose Pare, Lister, Semmelweis, Pasteur, Walter Reed; you could name them by

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the dozens. Progress is achieved by going outside customary and usual procedures. It derives from the freedom to experiment and to innovate. In this present malpractice climate, it is doubtful whether anybody would attempt such a procedure as a heart transplant for the first time in the United States today.

Public officials bear the responsibility in their duty to look after the general welfare of the state. I would like at this point to commend in the highest possible terms the attitude of the legislature and the insurance commissioner for their understanding of our problems. We have attempted to give the fullest explanations, and they have been most sympathetic and cooperative.

A third area of responsibility is borne by the insurance companies. In the past years they have had many problems; their vitally important reserves in practically all casualty fields have been reduced drastically by the recession and the decline in the stock market. This has been coupled by increasing payouts in professional liability insurance. But I have been distressed by the attitude of many insurance company representatives, who deny that malpractice is an insurance problem. I say if they deny their responsibility to the general public and do nothing to prevent a situation where doctors can no longer practice freely; they are inviting takeover not only in this field, but in all fields of their operation, by the federal government. The Executive Council has been puzzled by the reluctance of the insurance carriers to disclose their loss record and projected claims for our examination. Certainly they do not improve their credibility by such actions. This has not been confined to South Carolina. Robert E. Cartwright, the President of the American Trial Lawyers Association stated at the National Conference on Malpractice in Arlington last March that in 1974, malpractice payouts in California were approximately \$30 million — \$7.7 million in verdicts and \$22.3 million in settlements. If you divide that by the approximately 40,000 doctors practicing in California, you get \$750 per doctor. The average annual premium in California is \$3500. Mr. Cartwright asks along with several others, "Where did the balance of this premium dollar go?" In a recent review of an application for a rate increase by the largest malpractice carrier in North Carolina, the State Insurance Commissioner, John R. Ingram, made some significant findings. He reported that the company's actual paid losses and expenses from 1956 to 1974 amounted to less than 20% of the total written premiums and that its reserves and its reserve loss expenses were overstated by 40%. We believe that the insurance industry must recognize that its business is geared to the pub-



Pro-Banthine®

brand of
propantheline bromide

Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

Contraindications: Glaucoma, obstructive disease of the gastrointestinal tract, obstructive uropathy, intestinal atony, toxic megacolon, hiatal hernia associated with reflux esophagitis, or unstable cardiovascular adjustment in acute hemorrhage.

Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

Overdosage may cause a curare-like action, with loss of voluntary muscle control. For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and this possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evidenced by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

SEARLE

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Pro-Banthine[®] (propantheline bromide)

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option
in peptic
ulcer

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Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

makes sense in edema.*

Neither inconvenient, unpalatable, expensive potassium supplements nor special K⁺ rich diets are needed as a rule. Just 'Dyazide' once or twice daily for control of edema. Serum K⁺ and BUN should be checked periodically (see Warnings section).

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Indications: *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—

both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy

patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F Co., Carolina, P.R. 00630
Subsidiary of SmithKline Corporation



'Dyazide' gets excess water and salt out and helps keep essential potassium in.



Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

ound useful in the management of vertigo* associated with
ases affecting the vestibular system.

in relieve nausea and vomiting often associated with vertigo.*

usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.

so available as Antivert (meclizine HCl) 12.5 mg. scored
ts, for dosage convenience and flexibility.

ntivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for
ea, vomiting and dizziness associated with motion sickness.

SUMMARY OF PRESCRIBING INFORMATION

DICATIONS. Based on a review of this drug by the National Academy of
Sciences—National Research Council and/or other information, FDA has classified
indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with
motion sickness.

Probably Effective: Management of vertigo associated with diseases affecting the
vestibular system.

onal classification of the less than effective indications requires further
investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during preg-
nancy or to women who may become pregnant is contraindicated in view of the
teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation
has produced cleft palate in the offspring. Limited studies using doses of over 100 mg/
kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate.
Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hyper-
sensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients
should be warned of this possibility and cautioned against driving a car or operating
dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children
have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred
vision have been reported.

More detailed professional information available on
request.

ROERIG *Pfizer*
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert[®]/25
(meclizine HCl) 25 mg. Tablets
for vertigo*



**When the focus is on bronchitis due to
susceptible strains of *H. influenzae* and pneumococci***

Rondomycin[®] 300 mg.
[methacycline HCl] Capsules

Delivers from the very first dose:

**Studies show that after the first dose serum levels rapidly rise above
minimum *in vitro* inhibitory concentrations**

*Since many strains are known to be resistant, routine sensitivity testing is recommended.

Rondomycin[®]

methacycline HCl

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines.

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.** **Usage in pregnancy.** (See above **WARNINGS** about use during tooth development.) Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in bone growth rate observed in premature infants given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, their tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis. Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

CAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months. Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above. (See **WARNINGS**).

Neutropenia: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, laryngitis, exacerbation of systemic lupus erythematosus.

Infants: bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Adverse effects: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. For severe infections, an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea. In uncomplicated gonorrhea, when penicillin is contraindicated, 'Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule. 900 mg initially, followed by 300 mg daily for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of 'Rondomycin' (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug 1 hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding. In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

APPLIED: 'Rondomycin' (methacycline HCl): 150 mg and 300 mg capsules; syrup containing 75 mg/5 cc methacycline HCl.

For prescribing, consult package circular or latest PDR information.

Rev. 6/73

WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512

lic interest, and that it has a duty to the public, a responsibility to the public and an accountability to the public. This includes full details of premiums collected, the reserves set up, the investment of their reserve, the company investment portfolio, and the ratio of premiums collected to payouts.

The legal profession also has a responsibility. We depend on them for the interpretation and administration of our laws and our court system since most judges were once lawyers. Although the contingency fee system is open to many abuses, it is the only system that give a poor person his right to have a day in court that would be impossible otherwise. Moreover, a really competent trial lawyer discourages far more malpractice cases than he tries, for a very simple reason. In an extended malpractice suit, a lawyer may be forced to spend up to \$40,000 to \$50,000 of his own money preparing and pursuing the case. For very practical reasons he cannot afford to try many malpractice cases which he does not win. On the other hand, there are many abuses. A California study by the Imperial Insurance Co. of Los Angeles, of 565 closed claims from 4 states over a 4 year period, showed that the total amount paid to plaintiff's attorneys was 5 times the amount paid to defense attorneys. Furthermore, 50% of the dollars paid to plaintiff's attorneys went to 6 lawyers and involved only 2% of the claims.

Finally, we come to the responsibility of the medical profession. If we are to ask the people of South Carolina to help us with our very real problems of obtaining professional liability coverages, we must do everything in our power to insure that the practice of medicine in South Carolina is maintained with the highest possible standards. Several legislators as well as newspaper and television commentators have already praised us for attempting to set up tighter disciplinary controls as one of the necessary prerequisites for getting professional liability legislation. At the National Conference of Medical Malpractice which I attended in March 1975, in Arlington, Virginia, the necessity for improved medical self discipline was stressed by several state legislators from Florida, Oregon, New York, and California as a vital component of professional liability legislation which they were enacting. It was strongly stressed by the President of the American Trial Lawyers Association and many other physicians, insurance men, and representatives of consumer organizations.

All doctors can agree I believe, that if we are to be disciplined by anyone it had better be by ourselves. The one remaining insurance underwriter is threatening to withdraw from the state if more favorable conditions are not available by July 1, 1975. The crisis is definitely facing us.

Your practice and that of every other South Carolina doctor is at stake.

The second major event which I would like to discuss is the proposed South Carolina Rural Health Delivery System. Since your approval of this project last December, we have disseminated information about this plan widely to state and national legislators, hospitals, foundations, and all other people interested in this problem. Our committee has met and laid down basic guidelines for implementation of this plan when money for the feasibility survey becomes available. We approved retaining American Health Systems, Inc. in developing the feasibility study. We have received already pledges and donations totaling almost \$6,000. A cooperative effort between South Carolina Medical Association and South Carolina Hospital Association has been instituted in order to obtain funding from the Duke Foundation and the Self Foundation. Attempts are being made to obtain funds from the Robert Wood Johnson Foundation. Although approximately 40 other foundations have been approached, they have been unable to provide us any money because of unfavorable financial conditions or previous commitments. A possible later source of help is the Rural Health Delivery Act of 1975 (HR5236). One of the most encouraging factors has been the support of the medical profession. Not only have the members of the committee spent long hours on this project, but several county medical societies and individual doctors have contributed several hundred dollars to this project.

I would urge every member of the South Carolina Medical Association to contribute to the South Carolina Institute for Medical Education and Research in order that we may reach our goal as soon as possible. If the South Carolina Medical Association can solve this problem, it will demonstrate louder than any other action that we doctors are interested in providing health care for all people. If we can do this job, we will know 1) it will be satisfactory to both patient and doctor; 2) it will minimize third party interference; and 3) it will show that doctors can and should provide leadership in solving health problems.

What future actions should the South Carolina Medical Association take? I do not have a simple answer to all our problems or to that question, but I am reminded of Alice in Wonderland after falling down the rabbit hole, undergoing several terrifying experiences, and finally losing her way, she approached the Cheshire cat, who had the rather maddening habit of appearing and disappearing at will. Alice asked him, "Do tell me, please — which way I ought to go?" And the cat replied, "That depends a good deal on where you want to get to." I urge you to look

long and seriously at the report of the Long Range Planning Committee this year. Here we have the yeast from which many future actions for the good of the Association may grow. The committee is not all knowing and may not be right in some of its recommendations, but they have spent many hours thinking about the good of all of us.

Most of their recommendations follow the consistent pattern of making the Association more responsive to the individual member and improving communication. As long as one councilor represents as much as 8 times as many doctors as another councilor, it will be hard to convince the average S.C.M.A. member that he is being treated fairly. The lifeblood of the Association are the committees. The increasing complexity of Association affairs demands that committees take on more work that has been done by the Executive Council in the past. The committees can examine problems in more detail than Council has time to do. Council in turn could decide on matters knowing that they have been thoroughly investigated. The proposal of additional officers to supervise committees and develop closer liaison with committees is a good one. I believe the time is coming when the scientific program of our annual meeting must consist of specialty sections in order to attract greater attendance and to provide leadership in post-graduate education. The Association should consider seriously setting aside 40-45 minutes on the first day of the annual meeting to allow candidates for the offices of the Association to present their platforms of goals to the House of Delegates. It is not fair to the House of Delegates to select leaders without knowing what they stand for. I say this as one who sneaked in on you, but the S. C. Medical Association is not a social club, it is a complex professional association. Being one of its leaders is about 1% honor and 99% hard work. To these recommendations I would like to leave you with one final statement. "Calvin Coolidge is dead." I do not mean to imply by this that you or I or any other member of the Association is 50 years out of date. However, what I do mean most emphatically, is that the old *laissez faire* free enterprise system is about as dead as Calvin Coolidge. After the businessmen of this country royally fouled things up to the point where the great depression of the thirties came, the American people rightly or wrongly decided that a number of limits had to be set, and that no business or profession would be allowed to do entirely their own thing, unhampered or unanswerable to the general public. This applied to medicine as well as any other profession; hopefully, someday it will apply to lawyers more strongly than it does today.

I urge you to participate in the work of the

Association. If you let George do it, George may do it wrong or never do it. If enough doctors let George do it, the SCMA, the AMA, and the freedom of all doctors will go the way of Brontosaurus. As Thomas Paine said "Those who enjoy the blessings of liberty must undergo the fatigue of supporting it." No association is stronger than its individual members. If you don't like the way things are being run, get busy and start changing them. Things will never be changed if you sit at home and sulk, or hide behind that old cliché, "My practice takes every minute of my time." This association has an almost unlimited potential, if its members will only work to help reach the goals.

I think this potential can be realized more easily because of the outstanding staff we have in Columbia. All of these people have been wonderful to me, but I would like to mention 3 in particular. If I told you all the things that Charlie Johnson did this past year, it would take the rest of this morning. His knowledge of law, business methods, and politics is amazing. He is a "can do" man, regardless of difficulties. Most of you know what Bill Mahon is doing from his numerous visits to the county medical societies. If any body can keep PSRO from becoming a non Anglo-Saxon four letter word Bill can do it. Finally I would like to pay tribute to Ron Harris, who has done double duty as director of public relations and as our most capable lobbyist in the state house. Ron has been practically full-time at the state house during the past six months when bills were being prepared and while the legislature has been in session. He has kept us well informed and in turn has provided our legislators with all information they have requested. He is respected by both doctors and legislators; and we are fortunate to have him.

I would also like to remind you that 1976 is an election year. Despite our remarkable progress in legislative relationships, with a minimal support from the SCMA members, there are a number of things that we need to consider. We need to support SOCPAC, the South Carolina Political Action Committee, more vigorously. I have been ashamed and embarrassed that a good part of the money that we have used to support candidates in South Carolina has come from other states through the generosity of AMPAC because we were too stingy and apathetic to do the job ourselves. Not only do we need to support AMPAC and SOCPAC more vigorously, in 1976, we need local physician support committees comprised of physicians and their wives who know the candidate, support the candidate, and go out and work for the candidate. This is the only way to establish lasting relationships with our legislators. On the county level, we need medical societies that will have meetings at

breakfasts and dinners with legislators on both a state and a national level on a regular basis. This medical Association at least once a year, preferably in early spring, should send the President, the Chairman of Council, and any other interested parties to meet with our Congressional delegation and talk with them on legislation of interest to the medical association. I am told that a Wednesday breakfast meeting is the ideal time. I hope the day will come soon when no doctor is so naive or apathetic not to realize that he is up to his neck in politics, whether or not he likes it. Any doctor who says he is above politics, is saying that being a responsible doctor and a responsible citizen is beneath his dignity.

Almost exactly 2,000 years ago that great and eloquent apostle, St. Paul awaited his execution by the tyrant Nero, in a lonely dirty prison near the Tiber River. During the last weeks of his life he wrote to his young and devoted follower, Timothy, the following words. "The time of my departure has come. I have fought the good fight, I have finished the race, I have kept the faith." My job has been much more humble than Paul's. My talents far, far less than his. Yet in a very small way, I hope that you will believe I have the right to say, "The time of my departure has come, I have fought the good fight, I have finished the race, I have kept the faith."

The Asheville School— one of the two "names to consider" in the South.

That's how **Business Week** talked about us. We're often compared with New England prep schools... and not just because of our rambling mountain campus and ivy covered buildings.

Here at The Asheville School, we place the emphasis on getting into the more selective colleges. From 9th thru 12th grades, we stress the development of study habits that permit our graduates to get higher grades... particularly as college freshmen. This is increasingly important today in gaining acceptance to graduate schools.

Better preparation is possible because of a highly motivated faculty and a low student/teacher ratio (10-12 Boys & Girls per class).

Other strong points include single dormitory rooms for each student, individually tailored study projects and an exciting mountaineering program. If you think your son ought to be college bound, write for more information. Even better, plan a visit to our campus.

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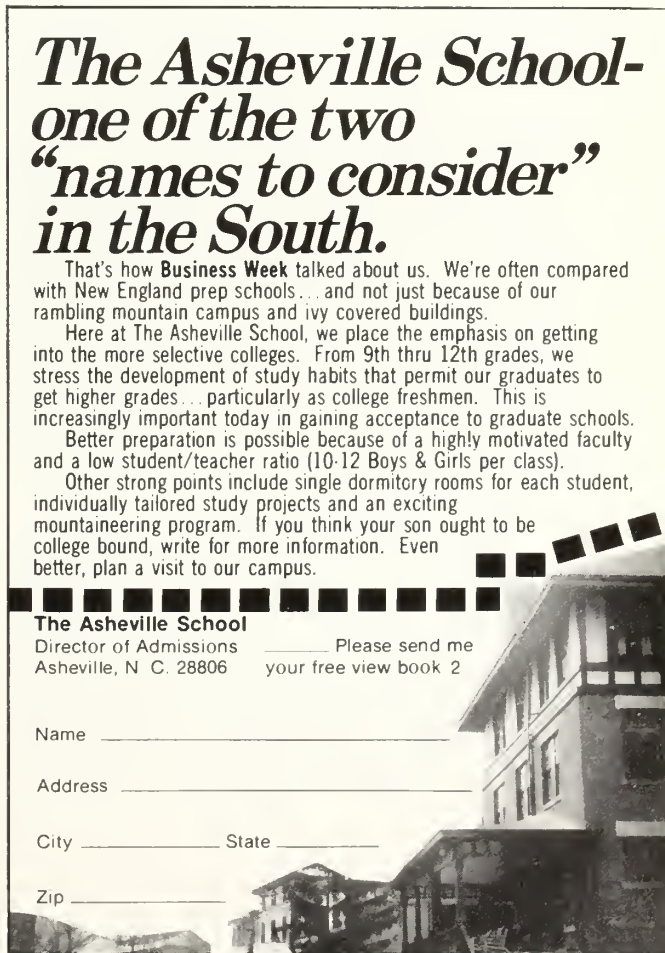
Director of Admissions _____ Please send me
Asheville, N. C. 28806 your free view book 2

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Ad Hoc Committee on Long Range Planning

This is a report of the Ad Hoc Committee on Long Range Planning of the South Carolina Medical Association for the year 1974-75 for submission to the House of Delegates at the annual meeting of the SCMA in May of 1975.

This committee has acted on the assumption that its function is to review the operation, background, functions and directions of the South Carolina Medical Association in all aspects and to make recommendations for future planning and projects. In this sense the committee is non-operative because recommendations will be reviewed and acted upon, or not acted upon, by the officers, Council, House of Delegates, and committees of the Association. During 1974-75 the committee has met four times.

Particular detail was paid to the present structure of the South Carolina Medical Association and the relationship of its constitution, bylaws, and governing bodies to the practicing physician of the state. In doing this it became apparent that there are inequities and inconsistencies in the present constitution which should be corrected. The committee particularly felt that the provision against soliciting votes for an office in the state society was inappropriate.

Recommendations: 1) It is recommended that the Committee on Constitution and Bylaws should review the entire document with the viewpoint to eliminate inequities and inconsistencies and to have a document which would have legal merit. If necessary, legal counsel should be employed to help in this.

In reviewing the constitution of Council, it was felt that the membership of this body did not reflect a fair distribution and representation for the practicing physicians of the state. The Councilor from one area could represent a considerably larger number of physicians than a Councilor from another area. Consequently, these areas should be revised to distribute the representation more equitably. It was also the feeling of the LRP Committee that the term of councilors was too long and did not permit the periodic infusion of new blood which is so essential to a vigorous responsive organization.

2) Recommendation: The membership of Council should provide an approximately equal representation of physician members for each councilor.

3) Recommendation: The terms of Council should not exceed two years with re-election not more than two times; such that the total term of a councilor could not exceed six years. The elections should be staggered so that not more than one-half Council would be elected yearly.

The committee reviewed the problems involved and the demands on the President of the SCMA from the viewpoint of his knowledge of the organization, the needs of the organization, and finally the ability of a practicing physician within this state (elected President) to respond to these demands. It was the feeling of the committee that the President should either serve for two years in order to provide proper continuity of service or, as an alternative method, the functional activities of the Presidential office be restructured in order that a second-tier executive structure be developed with the election of a President-Elect, Vice-President and Second Vice-President who are each designated to supervise a distinct segment of state association activities and who would report directly to the President. The President could then be able to devote his time to major matters and problems within the state and be relieved of considerable detail. Conceivably each of these offices could be advanced one step yearly so that by the time the Second Vice-President reached the Presidency, he would have been intimately connected with the state activities for three years and accordingly knowledgeable in association functions.

4) Recommendation: The functional activities of the SCMA should be restructured so that there will be a President-Elect, Vice-President, and Second Vice-President with specific areas of responsibility and reporting directly to the President.

5) Recommendation: The duties of committees should be delineated, preferably by present committee chairmen, to detail the duties and activities of these committees and their responsibilities. The committee chairmen would then report to the Vice-President supervising that area as mentioned above. Committee meetings should also have staff assistance for secretarial and other functions.

In conjunction with the decreased term of office for the councilor, the committee feels that the term of delegates from the county societies to the SCMA should also be limited to some degree. A three year term renewable not more than once, for the delegates would be desirable, in the committee's opinion.

6) Recommendation: The term of office of the delegate from the county society to the SCMA should not exceed three years and the delegate should not be eligible for election more than once so that the total term of office does not exceed six years.

7) Recommendation: The committee endorses

the action by the SCMA in requesting the limitation of length of service on all Boards and Commissions of South Carolina at the state legislative level and recommends that this be actively pursued.

The committee feels that mechanisms for possible discipline and/or censure of the practicing physician are needed. The violation of good medical standards or the lowering of medical ethics reflects on all. In this regard the State Board of Medical Licensure can plan an important part. On the other hand the medical society, itself, can serve if due safeguards are observed.

8) Recommendation: A formal review of medical practice may be required at time of license renewal. In addition to recommendations from such bodies as the county societies, hospital medical staffs, or specialty medical groups, there may be a requirement that the physician submit medical certification that he is capable of continuing medical practice. An alternative suggestion would be that the SCMA assume more specific disciplinary and regulatory functions in a fashion similar to that of the South Carolina Bar.

In South Carolina as in many other states the practice of medicine has become increasingly specialized and, therefore, a state society based only upon the needs and goals of the family practice of medicine would necessarily be less attractive to those in specialty or academic medicine. There is provision for component societies within the constitution of the SCMA, however, in practice, this has been limited. Only county medical societies have been members, with the recent exception of student physicians as a group.

9) Recommendation: It is proposed that specialty sections as component parts of the state society with delegates having a vote should be initiated. This would imply that specialty societies would be encouraged to present scientific as well as administrative programs at the time of the annual meeting of the SCMA.

10) Recommendation: The committee feels that continuing medical education can only be of benefit to the practicing physician and therefore recommends that a specific level of CME credits be necessary for continued state society membership and possibly even for relicensure. Concomitant with this objective, there should be workshops and programs on specific topics held conjointly with the state meetings and also within various areas of the state such that continuing medical education credit could be obtained by the physician with a minimum loss of practice

time.

11) Recommendation: The committee feels that the annual meetings of the SCMA should be held in geographically diverse areas of the state on a rotational basis, if at all possible. It is understood that logistic problems of holding the meeting are real; however, it should be possible to hold the state meeting other than at Myrtle Beach.

The mid-winter meeting of the society should be held in a location which contrasts geographically from that of the annual meeting.

12) The committee feels that there is a need for critical review of the News-letter of the SCMA and other communications to the membership. It is felt within the committee that the present format does not serve the needs of the membership. Publication of Society business in the South Carolina Medical Journal is often too delayed to be effective. Committee reports and actions at the mid-winter meeting should be distributed to the membership within a reasonable period. The minutes of the meetings of Council should be made available to the membership.

13) Recommendation: The Committee on Long Range Planning recommends that there be a retreat or other similar meeting of the officers of the State Medical Society together with committee chairmen shortly after taking office. Plans can be made, problems discussed, and actions taken which could make a coordinated approach to society needs. It is also recommended that the state leadership should meet with Presidents of the County Medical Societies in a group and utilize state and national resources to present pertinent information to these leaders. This could logically be a one or two day meeting held within the state and could be known as a "State Leadership Conference."

14) Recommendation: The committee feels that past Presidents should be restricted in membership and vote in the House of Delegates. The influence of the past Presidents should be felt as advisors in committee activities and in planning functions, rather than as an actual delegate with voting power.

15) Recommendation: The committee finally feels that the Ad Hoc Committee on Long Range Planning should be continued and that in the future it focus more specifically on the future needs of the Association.

E. Arthur Dreskin, M.D.
Chairman

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PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

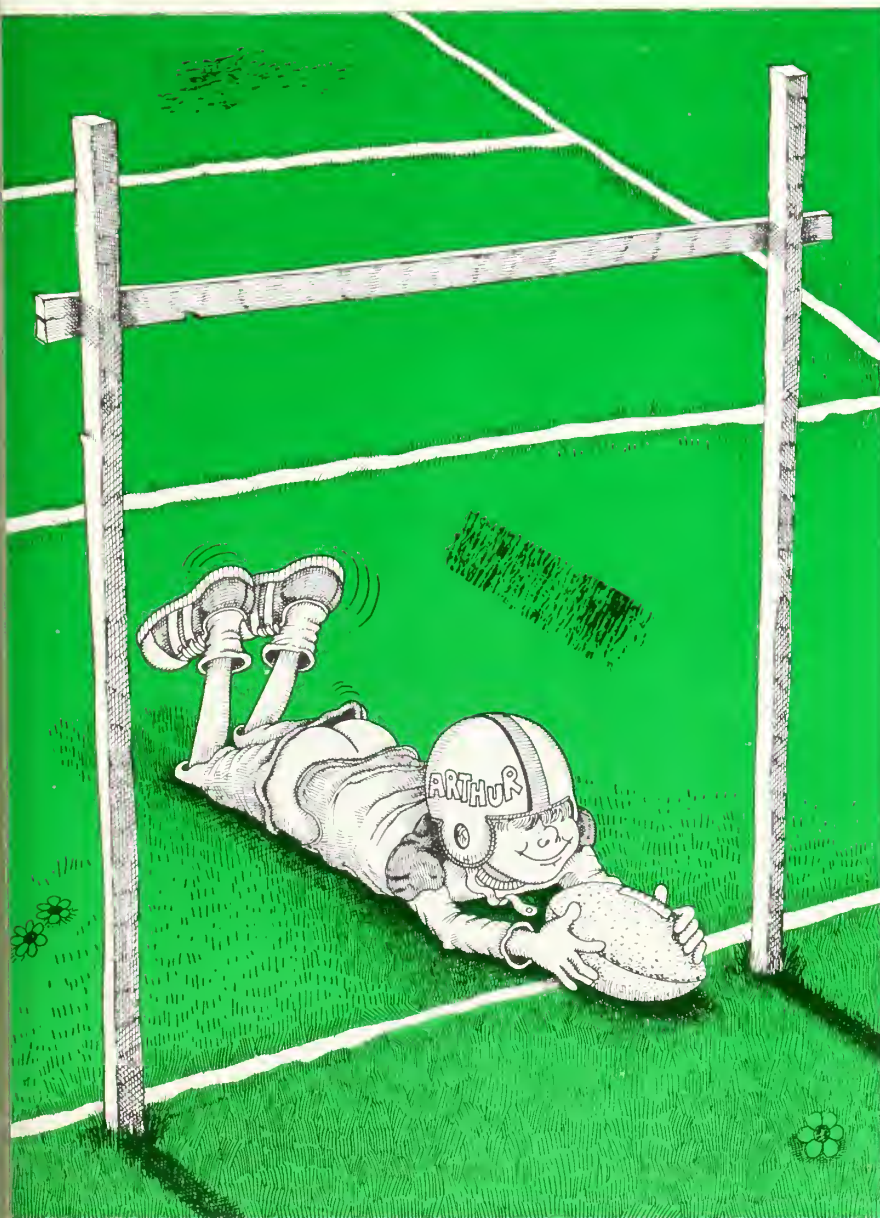
Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

ROERIG 

A division of Pfizer Pharmaceuticals
New York, New York 10017

WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies*. Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

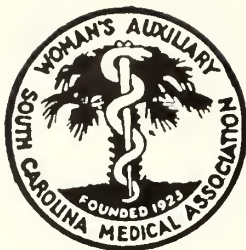
ROERIG *Pfizer*

A division of Pfizer Pharmaceuticals
New York, New York 10017

NSN 6505-00-148-6967

**Pinworms, roundworms controlled
with a single, non-staining dose of
ANTIMINTH[®]
(pyrantel pamoate)**

equivalent to 50 mg. pyrantel/ml.
ORAL SUSPENSION



WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION

Introducing a New President

The new President of the Woman's Auxiliary to SCMA is Sara Shingler, Mrs. John Monroe Shingler, Jr., of Spartanburg. She was installed at the Woman's Auxiliary Convention held in Myrtle Beach in May.

Mrs. Shingler was born in Rock Hill and attended Rock Hill High School, Winthrop College, and received a B.S. in Nursing from the University of South Carolina.

In service to the Auxiliary, Mrs. Shingler has been President and, most recently, Historian of the Spartanburg County Auxiliary. On the State level, she has served on the State Auxiliary Board as Mental Health Chairman and Community Health Chairman, and Regionally as Vice-President, First Vice-President, and President-Elect.

She has to her credit many civic activities aside from the Auxiliary being very active in Trinity Methodist Church in Spartanburg as well as being a member of the S. C. Conference United Methodist Church Commission on Religion and Race. For many years Mrs. Shingler has been active in the PTA and is also a member of the Cema Chreitzberg Garden Club and the Spartanburg County Multi-Disciplinary Committee on Child Protection.

There, too, are husband Jack, an anesthesiologist, and four children to add to her list of interests: John III, a freshman at Wofford College, Lisa, a senior at



Mrs. Sara Shingler

Spartanburg High School, Alma, a ninth grade student at Carver Junior High School, and Helen, a sixth grade student at E. P. Todd Elementary School. Mrs. Shingler also finds time for reading, especially biographies of Presidents and Presidents' wives, and crewel embroidery and sewing.

The Woman's Auxiliary has a lot of energy and talent in its new President and will surely have again a most productive year.

Maybe the patient's self-diagnosis is right. He could have hay fever. But that bright red nasal mucosa, along with the thick discharge and excoriation around the nares, strongly suggests that the main problem is a cold. Hay fever or another form of allergic rhinitis may or may not be an underlying factor.

If a complete history and examination rule out allergic rhinitis, the long-term outlook will be a lot more favorable than his own "diagnosis" would have indicated.

But right now, whether he's got allergic rhinitis or a cold, he's suffering from the same irritat-

ing symptoms of drip, congestion and stuffiness. Try DIMETAPP EXTENTABS®. They're formulated to relieve these symptoms without much chance of causing drowsiness or overstimulation. Your patients will appreciate the 24-hour relief they can get from just one tablet every 12 hours.

Cold or



Allergy?

Whether it's a cold or an allergy, Dimetapp Extentabs® effectively relieve stuffiness, drip and congestion.

INDICATIONS: Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses such as the common cold, seasonal allergic rhinitis, rhinitis, conjunctivitis and otitis. In these cases, it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions, thereby affording relief from nasal stuffiness and postnasal drip.

CONTRAINDICATIONS: Hypersensitivity to antihistamines of the same chemical class. Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age. Because of its drying and thickening effect on the lower respiratory secretions, Dimetapp is not recommended in the treatment of bronchial asthma. Also, Dimetapp Extentabs are contraindicated in concurrent MAO inhibitor therapy.

WARNINGS: Use in children. In infants

and children, particularly acetaminophen in overdose may produce convulsions and death.

PRECAUTIONS: Administer with care to patients with cardiac or circulatory disorders, diabetes or hypertension. If the patient's blood pressure has been determined, he should be cautioned against engaging in strenuous or hazardous activities while driving a car or using machinery, etc. Patients receiving antihistamines should be warned against possible additive effects with CNS depressants.

Dimetapp Extentabs®

Dimetane® (brompheniramine maleate), 12 mg.; phenylephrine HCl, 15 mg.; phenylpropanolamine HCl, 15 mg.

When used as directed, Dimetapp Extentabs are safe and effective. However, reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash, urticaria, angioedema, and also fever and throat irritation. In severe cases, a widespread erythematous rash, fever, and membrane edema of the throat, including laryngeal edema, may occur. Frequency and duration of reactions to Dimetapp Extentabs may be increased by concurrent use of other CNS depressants and by concurrent use of MAO inhibitors. Dimetapp Extentabs are supplied in bottles of 100 and 500.

A-H ROBINS

A. H. Robins Company, Richmond, Va. 23220

when pain goes on... and on... and on—



For the patient with a terminal illness, PAIN past, present, and future can dominate his thoughts until it becomes almost an obsession. The more he is aware of the pain he is now experiencing, the more difficult it is to erase his memory of yesterday's pain, and to allay his fearful anticipation of tomorrow's pain.


Surely the last thing this patient needs is an analgesic containing caffeine to stimulate the senses and heighten pain awareness. A far more logical choice is Phenaphen with Codeine. The sensible formula provides $\frac{1}{4}$ grain of phenobarbital to take the nervous "edge" off, so the rest of the formula can help control the pain more effectively. Don't you agree, Doctor, that psychic distress is an important factor in most of your terminal and long-term convalescent patients?

the analgesic formula that calms instead of caffeinates

Phenaphen[®] with Codeine

Phenaphen with Codeine No. 2, 3, or 4 contains: Phenobarbital ($\frac{1}{4}$ gr.), 16.2 mg (warning: may be habit forming); Aspirin ($2\frac{1}{2}$ gr.), 162.0 mg; Phenacetin (3 gr.), 194.0 mg; Codeine phosphate, $\frac{1}{4}$ gr (No. 2), $\frac{1}{2}$ gr. (No. 3) or 1 gr. (No. 4) (warning: may be habit forming).

Indications: Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products, excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.

 Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on written or oral prescription and may be refilled 5 times within 6 months, unless restricted by state law.

A. H. Robins Company, Richmond, Va. **A·H·ROBINS**

In patients with chronic or frequently recurrent urinary tract infections

Bactrim^{T.M.} outperforms ampicillin.

In new multicenter studies a higher percentage of Bactrim-treated patients maintained clear cultures for four, six and eight weeks.

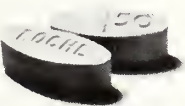
See charts on following page for details of studies.



For chronic cystitis or pyelonephritis evidenced by persistent bacteriuria, frequently recurrent infections or infections associated with urinary tract complications, when infection is due to susceptible organisms.

Bactrim^{T.M.}

(80 mg trimethoprim/400 mg sulfamethoxazole)



Before prescribing, please consult complete product information, a summary of which follows:

INDICATIONS: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus morganii*.

Note: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy, "Intermediate susceptibility" also indicates a likely response and "Resistant" that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. Data are insufficient to recommend use in infants and children under 12.

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

DOSAGE: Not recommended for children under 12. Usual adult dosage: 2 tablets b.i.d. for 10 to 14 days. For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	2 tablets every 24 hours
Below 15	Use not recommended

Supplied: Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10.



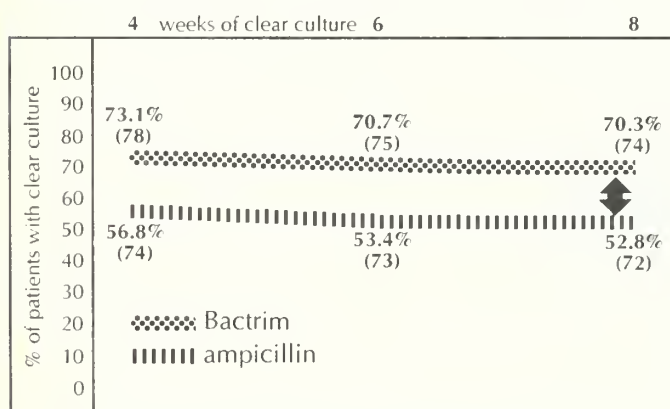
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

10 Shattuck Street
Boston Massachusetts 02115

In new multicenter studies
of patients with chronic or frequently
recurrent urinary tract infections

BactrimTM (80 mg trimethoprim/400 mg sulfamethoxazole) outperforms ampicillin

Bactrim vs ampicillin. 10-day therapy. 157 patients.



Criterion for clear culture: 1000 or fewer organisms/ml of urine.
Numbers in parentheses: No. of patients evaluated for this time period.

17.5% The Bactrim plus.

Patients maintaining clear cultures for 8 weeks

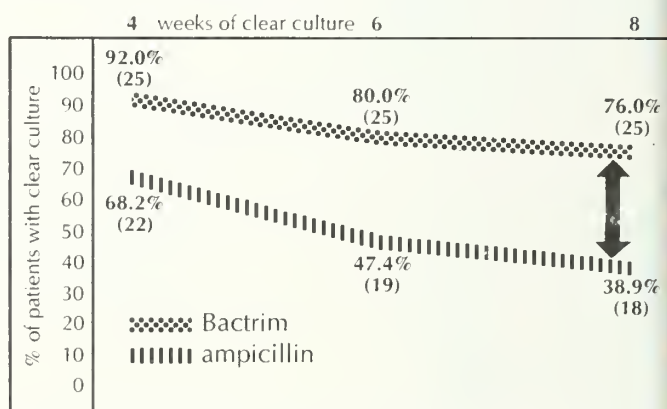
Bactrim: 70.3%

ampicillin: 52.8%

In two multiclinic, double-blind studies of patients with chronic or frequently recurrent urinary tract infections, Bactrim maintained a higher rate of clear cultures than ampicillin. All patients had "significant bacteriuria" (100,000 or more organisms/ml of urine) on two consecutive pretreatment cultures; many had previously undergone multiple treatment programs and/or surgery. Organisms were *E. coli* and *Proteus mirabilis*.

Side effects were relatively mild (e.g., nausea,

Bactrim vs ampicillin. 28-day therapy.* 53 patients.



Criterion for clear culture: 1000 or fewer organisms/ml of urine.
Numbers in parentheses: No. of patients evaluated for this time period.

37.1% The Bactrim plus.

Patients maintaining clear cultures for 8 weeks

Bactrim: 76.0%

ampicillin: 38.9%

vomiting, rash), but more serious side effects can occur with the agents studied. Please consult the manufacturers' product information for all warnings, precautions, contraindications and adverse reactions.

*While the usual therapy regimen for Bactrim is 10 to 14 days, patients with chronic urinary tract infections can be and are treated for substantially longer periods with standard agents such as ampicillin. These studies, therefore, include both 10-day and 28-day courses of therapy. In both studies dosage was one 500-mg ampicillin capsule q.i.d. or two Bactrim tablets b.i.d. plus placebos to make each drug regimen appear identical.



Please see preceding page for summary
of product information.

THE JOURNAL

SOUTH CAROLINA MEDICAL ASSOCIATION

THE FRANCIS A. COUNTRYMAN
LIBRARY OF MEDICINE
BOSTON

SEP 15 1975

MEDICINE'S "FUTURE SHOCK"

RUSSIAN MEDICINE

POSSESSION OF REGULATED SUBSTANCES

CHONDROITIN-SULFATURIA

VOLUME 71

JULY 1975

NUMBER 7

BECOTIN®

Vitamin B Complex

BECOTIN® with VITAMIN C

Vitamin B Complex with Vitamin C

BECOTIN®-T

Vitamin B Complex with Vitamin C, Therapeutic

MI-CEBRIN®

Vitamins-Minerals

MI-CEBRIN T®

Vitamin-Minerals Therapeutic

AND A WIDE VARIETY OF OTHER PHARMACEUTICALS



DISTA PRODUCTS COMPANY
Division of Eli Lilly and Company
Indianapolis, Indiana 46206

Both often



Predominant
psychoneurotic
anxiety

Associated
depressive
symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor

neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

respond to one

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON

SEP 15 1975



Valium® (diazepam)

2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent

in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

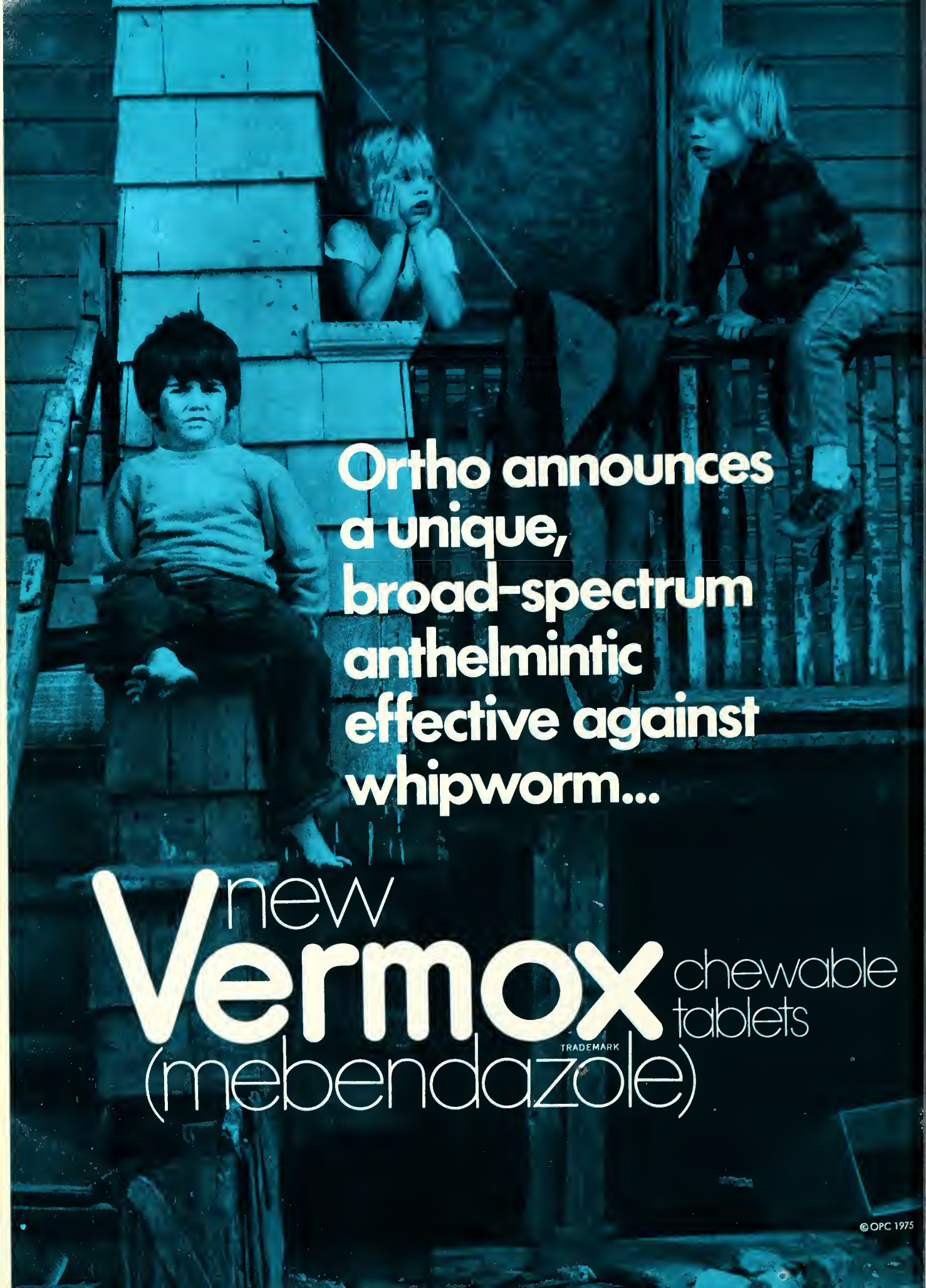
Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

A black and white photograph of three children on a wooden structure, possibly a playhouse or a porch. One child is sitting on a ledge on the left, looking towards the camera. Another child is leaning out from a window or opening in the center, looking out. A third child is standing on the right, looking away. The structure is made of wood and has a ladder-like element on the left.

**Ortho announces
a unique,
broad-spectrum
anthelmintic
effective against
whipworm...**

^{new}
Vermox TRADEMARK chewable
tablets
(mebendazole)

...and highly effective against roundworm, hookworm and pinworm in single or mixed infections



No dosage calculations — one simplified dosage,
regardless of weight or age[†]

whipworm, roundworm, hookworm and mixed infections:

1 chewable tablet b.i.d. for 3 consecutive days

pinworm: 1 chewable tablet

If the patient is not cured three weeks after treatment, a second course of treatment is advised.

highly effective

	Mean Cure Rate (Range)	Mean Egg Reduction (Range)	No. Patients	No. Studies
Whipworm (<i>Trichuris</i>)	68% (61-75%)	93% (70-99%)	211	(5)
Roundworm (<i>Ascaris</i>)	98% (91-100%)	99.7% (99.5-100%)	101	(2)
Hookworm	96% (—)	99.9% (—)	23	(3)
Pinworm (<i>Enterobius</i>)	95% (90-100%)	——	524	(7)

simplicity of administration

patients can take the tablet at any time.
It can be chewed, swallowed or crushed and mixed with food. No messy liquids to pour.

not a dye

new Vermox[®] (mebendazole) chewable tablets will not stain clothes, teeth, feces, toilet bowls, etc.

convenient

neither laxatives nor special diet required. Therapy does not interfere with daily activities.

well tolerated

transient symptoms of abdominal pain and diarrhea have occurred
in cases of massive infection and expulsion of worms.

Vermox has not been extensively studied in children under 2 years of age, and thus, the relative benefit/risk should be considered before treating these children. Vermox is contraindicated in pregnant women. (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Indications Vermox[®] (mebendazole) is indicated for the treatment of *Trichuris trichiura* (whipworm), *Enterobius vermicularis* (pinworm), *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed infections.

Efficacy varies in function of such factors as pre-existing diarrhea and gastrointestinal transit time, degree of infection and helminth strains. Efficacy rates derived from various studies are shown in the table below:

	<i>Trichuris</i>	<i>Ascaris</i>	Hookworm	Pinworm
cure rates mean (range)	68% (61-75%)	98% (91-100%)	96% —	95% (90-100%)
egg reduction mean (range)	93% (70-99%)	99.7% (99.5-100%)	99.9% —	— —

Contraindications Vermox is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

*TRADEMARK

Precautions **PREGNANCY:** Vermox has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since Vermox may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and administration The same dosage schedule applies to children and adults.

For control of trichuriasis, ascariasis, and hookworm infection, one tablet of Vermox is administered morning and evening on three consecutive days. For control of enterobiasis, a single tablet of Vermox is given.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

How supplied Vermox is available as tablets, each containing 100 mg of mebendazole, and is supplied in boxes of twelve tablets.

Ortho Pharmaceutical Corporation,
Raritan, New Jersey 08869



THE JOURNAL

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JULY, 1975 — VOL. 71, NO. 7

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Contributions of Original Articles

Length—Short articles of about 2,500 words (about 8 typewritten pages, double spaced) are preferred. Longer articles will defer to the shorter ones in schedule of publication.

Manuscripts should be typewritten, double spaced, and the original and a carbon copy submitted.

Illustrations—Ordinarily publication of 4 small illustrations or the equivalent accompanying an article will be paid for by The Journal. Any number beyond this must be paid for by the author except under unusual conditions. Illustrations should be sent as glossy prints or graphs in black ink with lettering large enough to show after reduction.

References—Should conform to the following order: surname and initials of author, title of article in small letters, name of periodical, with volume, page, month, day of month if weekly, and year—e.g.: Lee, G. S.: The heart rhythm following therapy with digitalis. Arch. Int. Med. 44:554, Dec. 1942. They should be listed numerically in order of appearance in the text. Standard abbreviation for journals should be used. Note that periods are not used with these abbreviations as indicated by the Index Medicus. Other abbreviations should be standard—e.g. mg, ml, Gm.

Reprints—Reprints will be made for the author at established rates.

Let somebody take care of you for a change.

You have enough to worry about taking care of all your patients without worrying about your financial security. Leave that to C & S Bank.

Our Trust Department is staffed with professionals who can help you with everything from personal trust services to pension and profit sharing plans. And we'll work with your attorney, accountant or underwriter to design the plan to fit your specific needs. So come in and talk to our Trust Department. And say "ah-h-h."

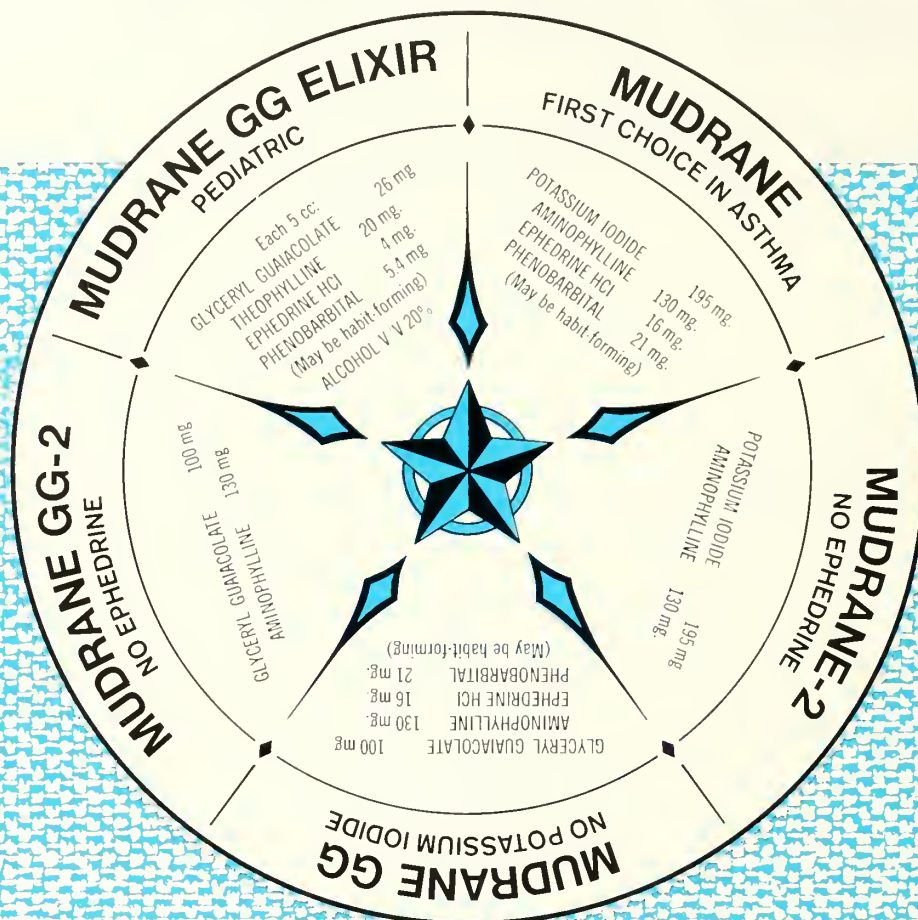
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MEDICINE'S "FUTURE SHOCK"

WILLIAM HARVEY HUNTER, M.D.*

People today are being overwhelmed by the sheer velocity of sociological and technological change, says Alvin Toffler in his brilliant *Future Shock*. He calls this tremendous cultural speed-up "a current so powerful . . . that it overturns institutions, shifts our values, and shrivels our roots."

We in medicine, perhaps more than anyone else, have been subjected to such a multitude of changes as to make it more and more difficult for us to separate the wheat from the chaff.

A constant stream of new literature on disease, diagnosis, and therapy; numerous new institutions active (or trying to be so) in the health field; reams of new legislation; the dissemination by the uncomprehending news media or varying degrees of knowledge and expectations concerning all of this activity explosion—all have combined into one geometric total that has left many of us ourselves in shock.

In the long run, however, the persons most apt to suffer from these major problems of "future shock" are not ourselves, but our patients. For our patients today, the greatest single medical problem in the United States is not the cost of medical care nor the malpractice problem. Rather, it is the desire of our patients to have capable physicians available to look after their health needs. Every patient wants,

and deserves, a medical advocate. As physicians we are our patients' advocates during illness; and so should we be their advocates in health planning.

Unfortunately, a great many people in this country have no such advocates, nor do they now have prospects of getting them. Instead of family physicians, these people are being offered nurse practitioners, physician assistants, or an emergency room number. Vague government plans envision H. M. O's that will give these people another number in an institution that will end up costing them four or five times what private medical care does, and the cost will be taken out of their pay checks as taxes.

So we all, physicians and patients alike, approach even greater shock, while the many facets of medical-care problems seem to multiply as fast as a gram negative bacillus in the blood stream.

Today the physician in private practice offers more people better medical care than the world has ever known. But he must often wonder what has gone wrong. Why is he faced with this voluminous amount of legislation from the halls of Congress? The United States has the third highest number of physicians per capita of any nation in the world; and a marked increase of medical student enrollment has been brought about by the efforts of the last Health Manpower bill, which will probably bring about a surplus of phy-

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sicians in the early 1980's. Yet the average American has no medical advocate of his own, and no simple easy entry to medical care. Today in the United States, this situation will be accepted by neither patients nor politicians.

The problem is obvious: a marked maldistribution of physicians both by geography and by specialty. But the diagnosis, although simple, leads to no simple therapy. We physicians must devise this treatment, and quickly, or someone in government is going to do it for us. Indeed, it is such a late hour in this particular crisis that it may well take all of us, private and public practitioners, working together to prevent further problems in medical care.

For this patient who is now in impending shock, perhaps a bit of history is now in order.

In 1970, The American Specialty Boards approved the 22nd specialty—the Family Physician. Now, we have the three educational steps for a practicing physician: undergraduate, medical school, and residency of three to five years, depending on the specialty. Our problem focuses on the residency programs, for the resident training of the M.D. obviously decides what kind of medicine the M.D. will practice and the place where the M.D. will practice is influenced strongly by the locale of his resident training.

At a time when the crying need is for Family Physicians, the medical schools (with a few notable exceptions) and the Congress (with one notable exception) have failed to provide the means for enough resident positions in Family Practice to accommodate the number of medical graduates who sincerely want such a residency.

Congress' notable exception was the Family Practice Training Act of 1971. But the American Association of Medical Colleges urged President Nixon to veto this Act, because the Act specified that the medical schools were to spend the money on Family Practice programs. In 1974, this pocket veto was ruled illegal by the

courts, but this was three years too late to help establish residency programs in Family Medicine. By this time, the appropriations were irretrievable.

However, the handwriting was on the wall. The mood of Congress and of the people was known even to the A. A. M. C. So then was conjured up the great subterfuge, "Primary Care"—and, even worse, "Primary Care Physicians." The reason for this subterfuge, of course, was to gain control of the money and of the residency programs which will get the dollars. So countless hours, both medical and bureaucratic, have been spent in attempts to define these terms. No agreement on such a definition has yet been reached. Furthermore, no one yet is sure who will be concerned with "Primary Care."

Recently, during a meeting in Chicago of The Council on Medical Specialty Societies, the Ob.-Gyn. people wanted to be considered as "Primary Care" physicians. They were voted down. Indeed a study group of the A. A. F. P. has recently stated that there is no such person as a "Primary Care Physician."

If a certain element in the A. A. M. C. has enough influence, these funds won't go to Family Practice residencies at all, but to some vague term of "Primary Care" which will probably include Internal Medicine and all of its sub-specialties, Pediatrics and all of its subspecialties, and then perhaps Family Practice. Why Surgery and Ob.-Gyn. and all of their sub-specialties aren't included, I don't know. Their claim to the "Primary Care" title, along with their cut of the pie, is as valid as the claims of Internal Medicine or Pediatrics. What we have here is an internecine medical struggle over the residency programs.

The patient and his desire for a physician may well be lost in such a struggle. Who is to be his medical advocate—a narrow specialist like the Hematologist or the Pediatric Cardiologist? After all, these specialists did much of their residencies in so-called "Primary Care."

These narrow specialties are vital and necessary, but the way they are presently mal-distributed is another of the factors conducive to "future shock."

Having served the past three years as a member of the National Advisory Council on Health Professions Education, I have been dismayed at the resident training distribution in the country. We are actually training more surgeons than Family Physicians.

Last year, the A. M. A. approached this problem by asking that 50% of the residencies be in Family Practice, Internal Medicine, and Pediatrics. But this is too little and perhaps too late. At this time, only 30% of U. S. physicians in the residency phase are in these specialties. And right now only 35% of our physicians are practicing in these fields, as compared to 72% in Great Britain. In fact, taking into consideration normal attrition, for us to have 50% of our physicians in these fields ten years from now would require 90% of all medical graduates to enter one of these three fields during the next ten years. The figures are even worse when we take into consideration the many narrow sub-specialties that spring out of Pediatric and Internal Medicine residencies. The Hematologist or the Pediatric Cardiologist certainly is not a "Primary Care Physician," whatever that term does mean.

We may as well face it: if we are talking about the physician who first sees the patient and continues to look after him, using consultations and referrals as necessary, then we are talking about Family Physicians. The problem, and hence the "shock," is that there are not enough F. P.'s, just as there aren't enough Internists, all because of a badly botched over-all residency program distribution.

If certain members of the A. A. M. C. had spent their energies four years ago on things other than blocking federal support of Family Practice programs, we would be better off today.

The one bright spot in this otherwise dismal picture has been the American

Academy of Family Physicians, an organization which has tried constantly, often against formidable opposition, to increase the number of Family Physicians. At present, there are 219 approved residencies in Family Practice, and, as of July 1, 1974, a total of 2,671 such residents in training. We expect these numbers to increase steadily over the next ten years.

In using the example of A. A. M. C.'s shortsightedness, I do not mean to place the major portion of the blame upon this organization, though it must assume its share. The medical schools, the Congress, H. E. W., specialty boards, specialty societies, the hospitals, and, yes, the private section of medicine all have a share of the blame for this muddle in which we find ourselves.

The problem is that the present residency programs in our country are not tailored to our people's needs. Furthermore, the so-called "Primary Care" movement is not going to answer these needs, and may indeed prolong the reaching of a solution. We should begin immediately to move towards motivating 50% of our medical graduates toward Family Practice residencies. For neither our patients nor our profession can any longer tolerate these conditions which have led to this serious case of "Future Shock."

The successes and partial successes of the present Health Manpower Act are evidence that the private and public sectors of medicine, along with the medical schools, *can* work together. One element of the cure is federal funding of residency programs, which is already a fact of life. A second element is the obvious responsibility of the medical schools for career guidance. The third factor in this problem-solving group is the private sector of medicine, with its advocacy for the patient.

This triad must come together and soon perform drastic surgery on our present residency program. We must restructure them into a responsible institution that will meet the needs of our people.

RUSSIAN MEDICINE

C. WARREN IRVIN, JR., M. D.*

As we would expect, medicine in ancient Russia is even less well-documented than in most European nations. Little information concerning science during this early period of Russian history is available, but it is known that both Islamic and Byzantine cultures were enjoyed in the capital city of Kiev. This included a scientific practice of medicine transmitted down from the earlier Greeks, but as the Tartars destroyed this beautiful river city its culture virtually disappeared. Some residue of medical information was recorded in the monasteries but as the monks did not teach, "scientific medicine" gradually died out. There was no medical education in Russia after this for many centuries. Beginning about the 15th century the first modern physicians were trained abroad, and only a handful were available. The number increased gradually until the 17th century when the first medical school was founded in 1654 in Moscow as "The Military Medical School." The name of this school gives some indication as to the reasons for the establishment of institutions for medical education. For many years all medicine was oriented to the military and in 1682 two military hospitals were built in Moscow.^{1,2}

Peter the Great exerted great influence on the Russian people and even today he is the one Czar who is admired by the post-revolutionary Soviet citizens. It was Peter who accelerated the westernization of Russia, but even though he encouraged the growth of medicine it was for the benefit of the military, and thus in 1706 he established the Chirurgical Academy at the Military Hospital in Moscow. This

was the first scientifically oriented medical training institution in this country. Europeans were brought in to staff the Academy and after this for many years foreign physicians played an important role in Russian medicine and culture. In 1715 hospitals were established in Petersburg and by 1730 seven physicians had been graduated in addition to eleven under-physicians. Following Peter's death, a transient decline in Russia occurred and even though Peter had brought in as many as 125 physicians, by 1740 this had decreased to 40. Later, Elizabeth and Catherine II encouraged medicine as well as other educational activities in the Soviet Union. Further progress, although seemingly pitifully small to us, did occur. By 1796 there were 299 physicians in the Soviet Union. Out of this number a few were native Russians.

In the late 18th century and in the early 19th century the rise in the Middle Class began, and with its appearance, there occurred some increase in educational possibilities in Russia. During this time the University of Moscow established a medical institution and later, in more remote areas, medical schools were founded, so that by the middle of the 19th century most of the Russian physicians were native born. During this period of time there remained a dominancy of the military and, even up until the late 19th century, military medicine was emphasized though this number of physicians for the total population remained quite small. Actually, in 1809 there were only 2,596 physicians for 35,000,000 people. And this number had not risen percentage-wise by a great deal throughout the remainder of the century.

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In 1864 the Zemstvos were established by the order of Czar Alexander. These assemblies were allowed to have some control over local affairs and they had responsibilities from the peasantry as well as the rising middle class and the land-owning gentry. At this time (shortly before the freeing of the Negroes in the South) the serfs were freed by the Czar. Pressure on the Central Government, however, abated somewhat and there was never allowed a national assembly. Yet these Zemstvos played a significant role for many years in local government and were the instrument for the providing of social and medical care for the general population. It was the Zemstvos that paid for the physician and that established hospitals in regional areas which for the first time cared for the entire population. During the next fifty years up to World War I, physicians employed in this manner played not only a sensitive role in the welfare of the general population but were also a vital part of the "Third Element." It was these Russian-educated young intelligentsia who influenced all of Russia toward a more revolutionary and left wing outlook. The dramatic role played by these native-born physicians as well as others is well known, and, even though in numbers they were a very small part of the total population, their influence in recognizing and correcting the inequality of Czarist Russia was paramount. The first all Russian medical organization was established in 1881 and called the Pirogov Medical Society in honor of a famous Russian military surgeon. We will have more to say of this interesting and humane intellectual later.

In spite of these tentative efforts, Russia was not able to develop in a democratic fashion and the autocracy of the Czar and the ruling class remained quite strong. The increase in the number of physicians was slow, due in part to the lack of educational opportunities for the peasantry to prepare themselves for admission to the few medical academies that

were available. In 1900 there were about 17,000 physicians in all of Russia and as late as 1912, one authority records 22,772 physicians and 28,500 fel'dshers. Another source³ states that by 1917, or the beginning of World War I, there were about 20,000 physicians in all of Russia. At that time there were 1,500 physicians graduating annually from 13 medical faculties and 5 medical schools for women. After the Glorious Revolution "the doors of the medical faculties of the Universities were flung open to the working class youth, and by 1922 the number of faculties had increased to 34."³ From this time until the onset of World War II, various changes in medical education occurred under the Soviet System. There was a gradual increase in the number of years required for total medical education beginning at about 4 and rising to 5 at the onset of World War II.

Graduate education beyond the secondary school level in Russia is somewhat different than in the United States. All Russians were required to have a basic education carrying them up to what would be about 10th grade of our high school level. Those who desire further educational opportunities may take two more years of secondary schooling following which they enter the University and institutes. Those entering medicine, as well as other professions, enter directly into the appropriate academy or university. Following World War II this period of training was increased to six years. The first years are similar for those studying medicine, dentistry, pharmacy and public health, and include not only the necessary scientific subjects but also two years of foreign language, literature, philosophy, and other cultural subjects, including, I'm sure, education in communism. In 1954 there were 63 medical, 4 dental, and 8 pharmaceutical institutes and by 1974, this had risen to 78 medical and 5 pharmaceutical institutes and 9 additional medical faculties at universities.⁴ In 1941 the number of medical per-

sonnel had reached 115,000 but this most probably includes fel'dshers and other physician assistants. By 1972, however, the number of first year students in Russia was 54,150. In 1974 there were 766,000 physicians in Russia, being a ratio of 35 physicians per 10,000 people. "The Soviet Union occupies the first place in the world for the size of its medical manpower. There are more physicians in the USSR than in the United States, England, and France together. Soviet Physicians make up about one-fourth of all the physicians in the world and nearly half of the European physicians."⁴

The Soviet Union since its establishment has taken very seriously its need to increase the medical care of the population. It has only been able to do this by educating the masses. In some areas of Russia where literacy was 1% in 1917, the rate was approximately 100% in 1974. We were told in Tashkent of these figures and proudly our interpreter recounted the story of Lenin ordering the establishment of the University in 1924. All the professors, etc., were imported into this remote "non-Russian" province from Moscow. At the present time 3 medical schools educate physicians using the local language and with local talent.

The Russians are extremely proud of their physicians. The number of fel'dshers who served the rural areas before adequate trained personnel were available has been rapidly decreasing. Although I do not have figures, it was our impression that these were being replaced by fully trained physicians throughout the entire Soviet Union. The Soviet physician has numerous opportunities for further educational experiences and training after graduation. If he is of the Honor group in his class, he may proceed directly into specialization or into teaching, in various institutes and other opportunities that are available to him. A physician may be assigned for a period of time to rural areas after graduation, but, it was our impression, he later may serve as he

wished in other areas. All physicians are virtually required to take supplementary education and after three years the physicians are allowed to spend up to three months in a teaching institute receiving full pay as well as supplemental income. Apparently almost all physicians avail themselves of this opportunity.

As early as 1954 it was stated "we consider the greatest achievement in medical education after the revolution has been the setting up of medical institutes in those outlying territories which were national minorities in the days of Czarist Russia and are now national republics with equal rights. In all the vast expanse of Kazakhstan there was before the revolution only one medical institute and only about 100 doctors. In Uzbekistan the Soviet Government has set up four medical institutes, and in Tadzhikistan the Avicenna Center Medical Institute has been created."⁵

In order to get the flavor of the culture and more specifically a subculture such as Russian medicine, it is necessary to acquaint oneself not only with the basic facts of history but also to savor the lives of its heroes and villains, develop an insight and empathy into its joys, failures, accomplishments, sorrows, and dabble a bit into its literature and art. Russia is a country born and accustomed to oppression. First, under the Czars and later under the Soviets, the people have suffered physically for all their generations. Peter gave them a shove, the intelligentsia gave them hope and turmoil, and the Soviet Regimen have given them tyranny, oppression, and perhaps finally some of the "good things of life." Against this background of Czars, oppression, poverty, famine, two devastating world wars, one followed by the "Glorious Revolution," the people have remained loyal to the land and to their heritage.

Yet, some of the heroes of Russian medicine were not Russians. Peter imported mainly Germans and Dutch and it was Catherine II who encouraged the

English. Doctor (Sir) James Wylie, an Edinburgh Graduate, was the head of the medical-surgical academy for 30 years; later on at the founding (1799) of the military medical academy of St. Petersburg, he also became its head. Other Englishmen held important posts at the same time. While Wylie was head of the Army Medical Academy, Dr. James Leighton had a similar post with the Navy, and Alexander Crichton for the Civil Department. Wylie, however, was the strongest of the three, and the best loved by the Russians. He truly reformed military medicine. He put an end to the neglect of the common soldier and he was wounded three times while serving at the front lines. By also taking care of the enemy he was decorated by many foreign countries as well as Russia. On his death, after 64 years in his adopted country, he was a very wealthy man. The majority of his fortune was bequeathed to the Czar who used it to establish a military hospital in Petersburg which still stands, Dr. Wylie's statue and all.

Another Englishman who had many adventures in Russia was Dr. Robert Lee. He along with Wylie was involved in the Czar Alexander's death at the Crimea. There has always been a great deal of conflicting opinion not only about the cause of his death but whether he did actually die at this time. The reports of Wylie and Lee seem to clearly indicate that he died from typhoid and did not abdicate surreptitiously.

But enough of foreign physicians, many fine Russian physicians began to appear in the middle of the 19th century. In 1854 during the Crimean War where Florence Nightingale became so famous for the care of the English soldiers, a Russian surgeon received similar fame for his care of not only the soldiers but the citizens of Sevastapol. Dr. N. I. Pirogov (1810-1881) is perhaps the most famous of the Russian hero surgeons. During the above-mentioned seige he was in charge of all the hospitals and it was under his

control that the Grand Duchess Elena Pavlovna, sister-in-law of the Czar, founded the wartime nursing services. Dr. Pirogov was not only a superb surgeon but also an educator with very modern ideas. He felt that education was not a class right or privilege but something that should be enjoyed by all citizens. He believed that knowledge should not only be scientific in nature, which he recognized was quite necessary, but also that the citizens should be educated with a broad culture. He even felt that the teachers should pay attention to the students and that they should evaluate and encourage individual personalities. These thoughts, which to us seem rather commonplace, were felt to be radical for the Russians. He was given the task of organizing and developing Russian education on a national scale but his ideas and efforts were too radical for the Czar, so he was finally relieved of all his public duties. He returned to the land and lived in seclusion on his country estate practicing medicine until his death in 1881. It was in this year that the Pirogov society was founded. He remains one of the honored pre-Soviet citizens.

Another Russian physician famous more for his short stories and plays lived in this era. His lifetime was rather short, actually 44 years, but Anton Chekhov is well recognized as one of the leading playwrights of the 19th century. His short stories are somewhat melancholy, but his descriptions of the tragedies that occur when people cannot communicate with each other are quite moving. Some of the stories involve medicine and physicians and are worthwhile reading today.

The most famous of all Russian physicians, at least in Western eyes, is Ivan Petrovich Pavlov (1849-1936). This great physician was able to span the pre-and the post-revolutionary epochs and was honored by both. Born in Ryazan and educated in the Ryazan Theological Seminary as the son of a priest, he received his final education in Petersburg Univer-

sity and the medical-surgical academy there. He was apparently 30 years old when his scientific activity began in the physiological laboratory of Dr. S. P. Botkin, who was a most famous physician of his time. In 1890 Pavlov became a professor at the Military Medical Academy and in 1891 also served as the head of the Physiology Department of the Institute of Experimental Medicine, this same institute which we visited while in Leningrad. Pavlov was recognized by many countries and was awarded many honorary degrees, as well as his becoming a member of numerous scientific societies and institutions. It is difficult for us to recall that "pre-Pavlovian physiology was of a primary analytic nature, basically investigating the work of separate isolated organs and tissues. The Pavlovian stage in the development of physiology is characterized by shift of the study of the activity of the organism as a whole coordinated with the function of its organs and the maintenance of all normal ties and relations between the organism and the external world." I did not realize that Pavlov's first work was related to the physiology of the cardiovascular system and, in particular, the mechanisms of reflex mechanism of blood pressure. But beginning in 1888, he dealt with the physiology of digestion and it was because of this outstanding work that he was awarded the Nobel Prize in 1904. However, it was after this that his scientific interest turned to the "doctrine of high nervous activity of animals and man and the work of the cerebral cortex." It was in this study that the conditioned reflex became well-known and is so closely associated with Pavlov's name. The Russians are truly proud of him and I am confident that they should be. It is of interest as we stood outside of his famous institution where he remained for some 45 years that it was not a statue of Pavlov we saw, but a statue of his dog.

Russian literature gives the student much insight into the health and welfare

of the nation. Tolstoy's *War and Peace* describes the pre-Wylie physician leaving the battlefield with Prince Andrew and remaining during his convalescence ignoring the needs of the common soldier. Dostoyevsky's psychological novels, *Crime and Punishment* and *Brothers Karamazov*, are interesting reading for physicians. In the post-World War I era, *Dr. Zhivago* is perhaps still the best novel, but the physician who reads Solzhenitsyn's *Cancer Ward* is shocked and depressed by the carelessness of the medical care described by this fearless man.

The best way to study Russian medicine is to visit and talk to Russian people and physicians. In September of this year, Dr. Frank O'Sheal and I were privileged to be able to visit Russia. We were fortunate enough to have arrangements made for our introduction through the National Institutes of Health and—our experiences might be of some interest to you. When we arrived in Moscow we were disappointed in that the Institute of Cardiology where we hoped to spend some time was closed for repairs, and we could not therefore visit this center of learning and training. However, we were welcomed by the Ministry of Health and were greeted by the expert on Soviet-American medicine. He kindly arranged for us to have the pre-arranged symposium with the Russian Cardiologist and Psychiatrist working the above-mentioned institute. We spent the following morning discussing medicine with them. They were frank, eager to obtain information from us, and did not appear to be reticent in telling us how medicine was practiced. The psychiatrist clearly indicated that they have emotional problems associated with cardiovascular disease and perhaps some of these might be related to the rather prolonged (we thought) hospitalization and care the patient had following a myocardial infarction. They were interested in our drugs and Dr. O'Sheal was able to talk at some length with a psychological colleague about their usages.

Perhaps our most outstanding visit occurred in "St. Petersburg" where we visited the Institute for Experimental Medicine and were greeted by the Chief of the Laboratory of Lipid Metabolism, Dr. Klimov. He spoke fluent English, was warm and friendly, and virtually took an entire morning showing us around the grounds as well as his laboratory. We had tea, cakes, and even some very fine liquor. Most of the assistants were women who also spoke fluent English and it was here that we took a picture standing under the statue of Pavlov's dog. It is impossible for me to judge the originality of his research but the quality of what was going on seemed very good to us and there was no difficulty in transmitting information about what he was doing. The time spent with this eminent scientist was rewarding in giving us a rich insight in the Russian medical research.

That same day we visited one of the large hospitals in Leningrad. We were given the privilege of going into the wards and actually seeing where patients were being treated. We looked at electrocardiograms and saw where the patients with myocardial infarctions were kept. No monitoring equipment was available, yet equipment to defibrillate patients was available. As a majority of the patients seemed to be in wards, I presumed that the patient in the opposite bed merely screamed and yelled when a Stokes-Adams type of seizure occurred and defibrillation was carried out by the appropriate personnel. One of the most interesting facets of our visit here was the fact that the Director of the Hospital, a surgeon, carried a stethoscope similar to ours but the cardiologist, a woman of late 40's or early 50's was still using a monaural stethoscope. She seemed rather embarrassed when I asked to look at it and examine it but seemed pleased to introduce me to an elderly male physician later on that morning who was carrying a similar one. All in all, we felt that medicine was reasonable in this hospital but

certainly the shiny equipment that is available in our hospitals was not in evidence.

Following our visits in Moscow and St. Petersburg, we were privileged to see the Spas in Sochi where many patients are sent for rehabilitation. We had been told in Moscow that some of the cardiac patients were sent there, but this is on an experimental basis because an ordinary person who arrives there and who has a heart attack creates a great problem for his referring physician. The physician has to pay for the patient's time and hospitalization as angina pectoris is normally a contraindication to taking the bath. It was only with great difficulty that I persuaded them I was healthy enough to be allowed to get in the tub, but after talking with physicians in several Institutes I was permitted to do this. After this, they seemed even more friendly and presented us with a small medal as a token of our visit. The medical treatment given in the Spa is not comparable to anything we have in this country.

In far away Tashkent, really in Oriental Russia, we visited a university hospital which appeared to be about 15 years old. Here we were met by a cardiologist who spoke fluent English and asked us about some of the meetings he was hoping to attend and knew about. He and his younger colleagues were very enthusiastic and discussed many things with us. The person they are most proud of in this hospital is a young surgeon who had received the Young Communist League Award for his work on renal transplant and chronic dialysis. Here we took pictures in the Dialysis Unit and talked to this very outstanding, pleasant young man of about 33. He told us that he had not had rejection in the 10 transplanted cases, but unfortunately when we asked him about his mortality, this was rather high.

In attempting to evaluate the place of the Russian doctor in the present Russian Society and political state, it is helpful to have some concept of the differences of

material goods and total income that the Russian citizen receives from his work as compared to the American, which is difficult to do. As we all know, total spendable income in America is far less than the salary that the worker receives. The term "take-home pay" is familiar to us all. In Russia little if any income tax is taken from the worker's salary. The figures from 1960-68 are probably no longer valid and we were told that in general Russian citizens do not pay income taxes. Some tax, however, is collected, particularly from single males, childless couples, and from income received from such things as private medical practice. The maximum tax collected in 1968 from a total family group income calculated on 500 rubles which is extremely high was 12%. Such things as private medical practice, which must be rather rare, were taxed at a higher rate, and 43% of 500 rubles in 1968 was the maximum amount allowed. This is still less than that in America. Nevertheless, the figure of *adding* approximately one third to the worker's salary for social welfare services including complete medical care seems to be fair. Even this and knowing the exchange rate of one ruble is equal to a \$1.30 makes comparison difficult. The following quotation might give some idea: "Public transportation fares of 3 to 5 kopeks (there are 100 kopecks to the ruble) must be balanced against private automobiles commanding twice the price of equivalent American cars, at the official exchange rate. If the Soviet housewife pays less than half the American price for a loaf of bread, she sometimes pays a good deal over American prices for the better meats. Housing absorbs not 25% of the Soviet worker's income, but typically less than 10%; food, on the other hand, often takes as much as two-thirds. The worker may save to buy a co-op apartment or to vacation in the Caucasus, but he has no need to save for his son's university education. As a rough criterion of what a Soviet income will obtain during the 1960's, earnings of 60

rubles per month appeared to be the minimum for sustaining an individual living alone in Moscow; it may have been somewhat less in other cities and towns."⁶

On several occasions we were told that the physician makes less than the worker. This apparently is true for all intellectual pursuits in Russia and does cause some concern. Nevertheless, there does not seem to be a paucity of people applying for such educational opportunities, with the possible exception of school teaching. The Russian honors the physician. He is proud of the role he is playing in the Soviet life at this time and I am sure must be proud of his role throughout the last 100 years as a part of the intelligentsia. This honor to the physician and probably also the fact that they encourage women to enter medicine (they encourage all women to work in some manner) is part of the reason that there is an adequate supply of applicants to the numerous positions available in the medical schools.

We were told that the physician makes approximately 150 rubles per month and this is compared to 300-350 rubles for industrial workers and compared to 500 to 550 that the head of a large industrial plant might receive. Actually skilled workers make almost as much as the top management. The physician's income of 150 rubles per month is somewhat misleading as they are apparently required only to work 5 hours a day. Most of them work more than this and receive additional income because of it. It should also be noted that all workers receive one month's paid vacation a year beginning at the initial time of employment.

In summary, it appears that Russian medicine is rapidly increasing in skills and in the number of well-trained personnel. When we consider that they have two and a half times as many physicians per person as we do in America that there are now very few areas in even rural Russia where good medical care is not available we must realize the great com-

RUSSIAN MEDICINE

mitment the Russian people have made to medical care for its citizens. Couple this with a high level of morale and the admiration of the physician by the people, one can hardly believe that Russian medicine will not continue to improve. The Russian government, as ours, has committed a large proportion of the national income for medical care. It appears they have directed this not to basic research

and exciting experiments such as heart transplants, but to public health measures and to providing adequate numbers of well-trained physicians for the entire society. It is a different approach to health care from what our people are accustomed to receiving, but one we may well be turning toward. At least in an autocratic society, the fear of "too many doctors" seems groundless.

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LEGAL PENALTIES FOR POSSESSION OF REGULATED SUBSTANCES

MARTIN H. KEELER, M. D.*

It is useful for physicians to be aware of the penalties for the possession of regulated drugs because patients and relatives of patients may request such information and physicians are sometimes asked to express opinions about the severity of the laws.

A South Carolina Law, 32-1510.49b Code of the Law of South Carolina, 1962, as amended, and a Federal Law, Public Law 91-513, 91st Congress, H.R. 18583, October 27, 1970, pertain to controlled substances. These laws pertain to dealing, prescription, and manufacture, as well as possession. This presentation will consider only possession because most of the questions and requests for opinions directed to physicians concern possession.

The laws penalize possession rather than use. If use were penalized only direct observation of use, which would be a rare event, or the analysis of blood or urine, which cannot be done without the consent of the individual, would constitute evidence. Obtaining blood and urine samples for purposes of criminal prosecution without consent would be forcing the individual to incriminate himself and thus unconstitutional.

The laws give broad discretion to the courts in determining sentence. There is no mandatory minimum sentence for any violation that is only possession. The laws

cannot be described as barbaric although, in the opinion of some, they permit the judges to be barbaric.

It is often argued that the record of a conviction is a severe penalty even if no sentence is imposed because such a record may interfere with educational or occupational opportunities. Both state and federal laws provide a method whereby even the record of a conviction may be avoided. The Court, before or after judgment, may, with the consent of the offender, substitute a special probation for a sentence. Upon satisfactory completion of this probation no offense has occurred in the eyes of the law. Even if found guilty by a jury, the offender may state, without fraud, that he has not been convicted of a crime. The conditions of the special probation are determined by the Court and may include participation in a treatment program. This special probation option may only be used once by any individual.

It may be argued that even having been arrested may be an embarrassment. The laws recognize this and provide that an individual who has completed a special probation satisfactorily may petition the Court to have his record expunged. If this is granted, the individual may, without fraud, deny arrest as well as conviction. Federal law limits the benefit of denying arrest to those who were under twenty-one at the time of offense. South Carolina law limits it to those who were under twenty-five at the time of the

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POSSESSION OF REGULATED SUBSTANCES

offense and excludes offenses involving heroin.

Federal law does not distinguish among drugs for purposes of maximum sentence for possession. A first offense may be penalized by up to one year in prison and/or a fine of up to five thousand dollars. These may be doubled for subsequent offenses. South Carolina, with some exceptions, provides for maximums of six months in prison and/or a fine of up to one thousand dollars for first offenses involving possession which may be doubled for subsequent offenses. Penalties for a first offense constituted by possession of less than one ounce of marijuana or ten grams of hashish are limited to three months in prison and/or a fine of up to one hundred dollars. These may be doubled for subsequent offenses. Penalties for possession of LSD or a non-medically used narcotic, almost always heroin, may be penalized by up to two years in prison

and or a fine of up to five thousand dollars. For second offenses involving these drugs the maximum prison term is three years. For third and subsequent offenses the maximum prison term is four years and the maximum fine is ten thousand dollars.

The penalties for manufacture, distribution, and sale of regulated substances can be more severe and, in some situations, mandatory minimum sentences are specified.

The laws are not "barbaric" although some may claim they permit the Courts to be so. The laws are not permissive because severe penalties can be applied. Attempts to limit the discretion of the courts in either direction, in my opinion, are unwise because the court and not the legislature is aware of all the factors involved when it is necessary to determine sentence.



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CHONDROITIN-4-SULFATURIA, CHONDROITIN-6-SULFATURIA

JAMES RICHARD BOWEN, M. D.*

In 1929, Morquio¹ and Brailsford² characterized a syndrome of dwarfism, knock knees, flat vertebra, platyspondyly, osteoporosis and multiple epiphyseal abnormalities. Ullrich³ described patients with corneal clouding in addition to the abnormalities described by Morquio and this has been called "Morquio-Ullrich Disease." Pedrini and co-workers⁴ discovered increased keratan sulfate in the urine of patients with Morquio-Ullrich disease and the disease was established to be a mucopolysaccharidosis. Subsequently abnormal quantities of mucopolysaccharides other than keratan sulfate have been found in the urine of cases of Morquio's Syndrome. Maroteaux and Lamy⁵ reported cases with an increase in chondroitin sulfate A (or C) as well as keratan sulfate in the urine. Robins and Associates⁶ and Kaplan and Associates⁷ reported increased excretion of keratan sulfate-chondroitin sulfate in Morquio's disease.

Norum⁸ reported a non-keratan sulfate-excreting Morquio's syndrome, and Danes and Grossman⁹ describe two cases that could represent non-keratan sulfate-excreting Morquio's syndrome.

This paper reports a case with the physical and roentgenologic features originally described by Morquio¹ and Brailsford² with excessive chondroitin-4-sulfaturia and chondroitin-6-sulfaturia.

CASE REPORT

E.G., a 17-year-old black male was a full term "normal" infant at birth. An adequate history of heritage could not be obtained. He gained weight slowly and had small extremities when compared to body size. At one year of age, there was a mild anterior protrusion of the sternum, a short neck, and thoracic kyphosis. He sat at 5 months, walked at 22 months, was bladder trained at 1

year and was bowel trained at 2½ years. As a child, he had multiple colds, measles, influenza, asthma, and often a nasal discharge. His mother reported him to have a "musty" odor in his breath. At 7 years old, he started public school and had marked thoracic kyphosis, lumbar lordosis, anterior protrusion of the sternum, genu valgum, pes planus, ulnar deviation of both wrists, and was shorter than his classmates. During grade school, mild muscular weakness was noted in the legs and dyspnea on exertion developed.

At 16 years of age (Fig. 1), he is 4'2" tall and has a head circumference of 54½ cm. The nose is broad and flattened at the base. There is mild protrusion of the lower part of the face. Multiple small corneal opacities are seen bilaterally by a slit lamp examination. Audiometry reveals a hearing loss of 20 decibels in the left ear and 62 decibels in the right ear and is of sensory-neural type. The neck is short, and flexion and extension is limited to 30 degrees. The teeth are small, have sharp cusps, have stippled-grayish enamel and there is an extra left upper canine. The sternum is markedly protuberant. There is thoracic kyphosis, lumbar lordosis, and flaring of the ribs. At the 3rd intercostal space along the left sternal border, there is a grade II/VI crescendo-decrescendo systolic murmur. The liver and spleen are not enlarged and no hernias are present. The pelvis is small and there is genu valgus (15 degrees) bilaterally. There is pes planus bilaterally and hallux valgus bilaterally. The elbows have a 30 degree flexion contracture bilaterally and the radius is 1½ cm. longer than the ulna bilaterally. The patient has an I.Q. of 88 and is classed as dull normal. There was no sensation to pinprick, vibration, touch, hot or cold below T2 on the right and T4 on the left. The muscles of the legs contract but will not resist gravity. The muscles of the upper extremity were normal. All cranial nerves were intact. There was no bladder control. Reflexes of the lower extremity were hyperactive and there were Babinski's bilaterally. The patient underwent a right hemilaminectomy of T1, 2, 3, removal (subtotal) of the posterior portion of the body of T2, and an autogenous bone graft from the iliac crest to the deformity. (One year post-operatively, the patient walks with a walker, has bladder control, and normal sensation.)

*Charleston, South Carolina



Fig. 1. The photographs were taken three weeks after surgery.

Red blood cells revealed poikilocytosis and microcytosis. Small metachromatic granules were noted in a majority of the polymorphaleukocytes, lymphocytes and monocytes. The serum alkaline phosphatase was 27.3 KAU. Electrocardiograms showed a sinus bradycardia and pulmonary function studies revealed severe restrictive lung disease.

X-ray films (Fig. 2) of the case were reviewed. The skull was large and the nose was depressed at the base. The anterior end of the ribs was irregular and the coracoid process of the scapula was expanded. The clavicles were normal. The surgical neck of the humerus had dorsal angulation. The epiphyses of both ulna and radius were expanded and the articular surfaces sloped toward each other. The proximal row of carpals is poorly ossified. The pelvis is narrow at the level of the acetabulum and there is flaring of the iliac crest. The pelvic configuration is long and narrow. The neck of the femur is short and wide, the capital epiphysis is wide and compressed, and there is coxa valga. There is mild genu valgum. The thoracic and upper lumbar vertebrae are flattened and have tongue-like areas of ossification extending anteriorly. L5 is flattened and hooked anteriorly. The intervertebral disc space is wide. No odontoid process could be observed by routine

X-ray film or tomograms of the cervical spine.

Biopsies of the apophysis of the iliac crest and skin were obtained (Fig. 3). The apophysis of the iliac crest revealed marked disorganization of growth zones and a disordered pattern of endochondral ossification. The superficial layers appeared normal. In the zone of hypertrophic cartilage cells the chondrocytes were in clumps rather than columns. The chondrocytes varied in size and shape and some were enlarged with vacuolated cytoplasm. Occasionally granules were seen in the cytoplasm of the chondrocytes. At the zone of ossification, the trabeculae of bone formation were irregular. The osteoclast and osteoblast appeared normal in number and size but occasionally granules were noted in the cytoplasm of osteocytes. Skin biopsies reveal granules in the cytoplasm of epithelial cells of the rete pegs. Electromicrographs show these granules clearly.

The urinary mucopolysaccharides were evaluated by cellulose acetate electrophoresis before and after treatment with testicular hyaluronidase (Wydase) and at various pHs. The total urinary mucopolysaccharides were 88.6 mg/1000 cc urine. The chondroitin-4-sulfate and chondroitin-6-sulfate excretion was two-thirds of the total mucopolysacchariduria. The major remaining mucopolysaccharide in the urine was hyaluronic acid.



Fig. 2. X-ray films of the case.

A small amount of keratan sulfate, heparatan sulfate and dermatan sulfate was also noted.

DISCUSSION

The clinical characteristics of Morquio's syndrome has been well described and the disease exists in two types—a keratan sulfate-excreting type and a non-keratan sulfate-excreting type.¹⁰ In the keratan sulfate-excreting type, the mucopolysacchariduria may be excessive as a child and diminish as one matures.^{11,12} Uronic acid-containing mucopolysacchariduria has been reported to be elevated in keratan sulfate-excreting Morquio's disease.⁷ Keratan sulfate and chondroitin-6-sulfate exist on the same protein complex which may contribute to this finding.¹³ Chondroitin-4-sulfate mucopolysacchariduria has been

described, but none of the cases had the clinical characteristics of Morquio's disease.^{14,15}

The case in this report appears to be a variant of Morquio's disease with increased urinary excretion of chondroitin-4-sulfate and chondroitin-6-sulfate.

SUMMARY

A case of chondroitin-4-sulfaturia, chondroitin-6-sulfaturia with the physical and roentgenologic features described by Morquio¹ and Brailsford² has been described. This represents an unusual case of mucopolysaccharide metabolism.

ACKNOWLEDGMENT

I am most grateful to Dr. Phanor L. Perot, Jr. and Dr. Samuel S. Spicer for assistance in evaluating this case.

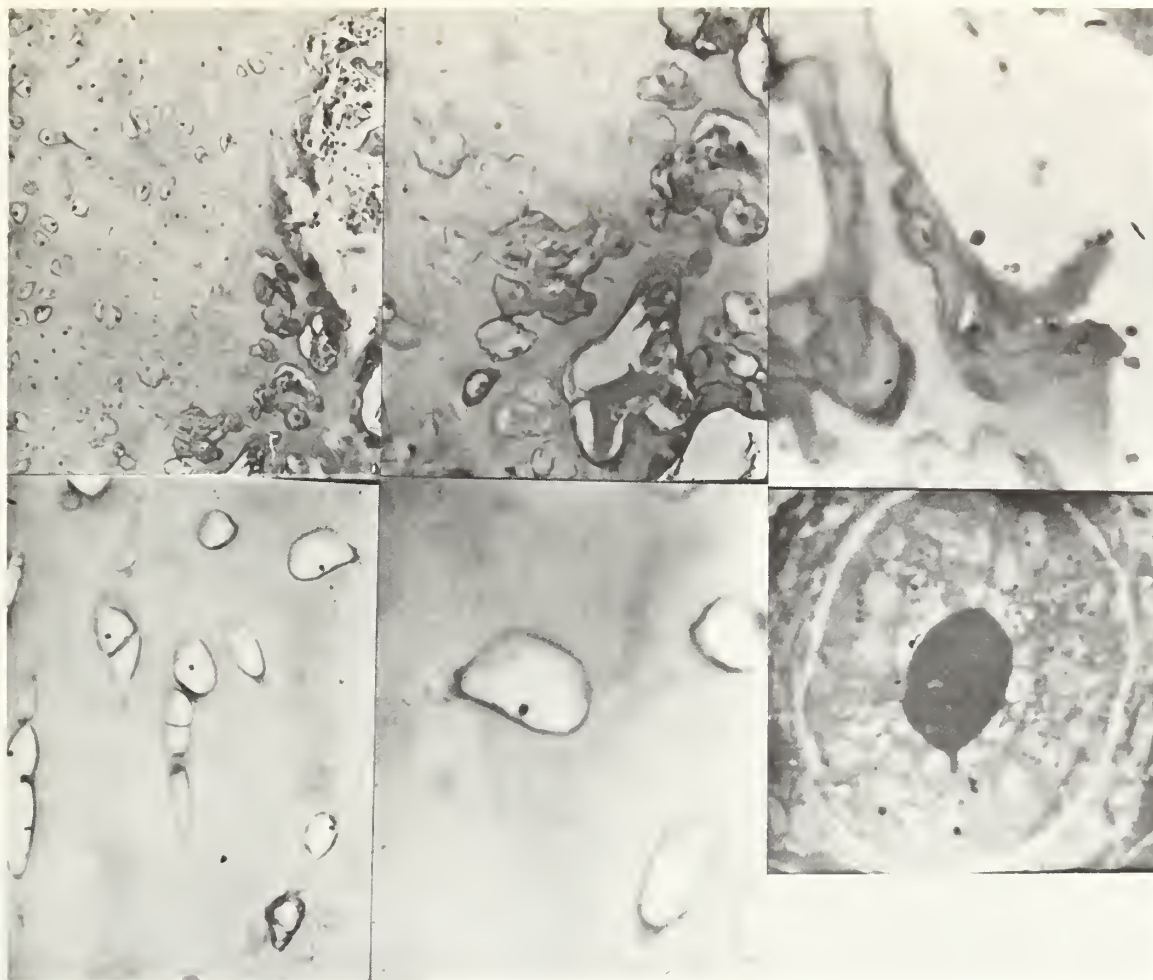


Fig. 3. The iliac crest apophysis (upper photomicrographs) show marked disorganization of the growth zones and abnormal patterns of endochondral ossification. The chondrocytes (lower left and lower middle photomicrographs) vary in size and have vacuolated cytoplasm. Epithelial cells of the skin (lower right electromicrograph) show granules in the cytoplasm.

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the weight of scientific opinion:

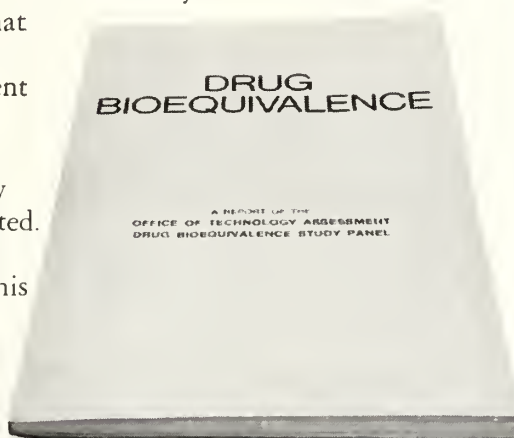
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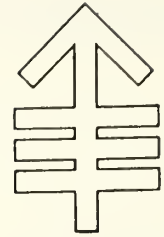


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CANCER TOPICS



ADRIAMYCIN AND BLEOMYCIN — REAL ADDITIONS TO CURRENT CHEMOTHERAPY

PAUL H. O'BRIEN, M.D.*

In 1972 we briefly reviewed the history of chemotherapy in the Journal of the South Carolina Medical Association.¹ It was emphasized that new insights in the cell cycle and the understanding of the molecular action of various products had improved the effectiveness of chemotherapy. There is understandable discouragement with chemotherapy in 1975, however, because of the relative infrequent nature of the cancers that are highly responsive to chemotherapy. To list those diseases highly responsive to chemotherapy, we have a group which cause no more than eight percent of cancer deaths.

TABLE I

Acute lymphocytic leukemia
Burkitt's lymphoma
Choriocarcinoma
Embryonal cancer
Testicular cancer
Ewing's sarcoma
Hodgkin's disease
Lymphosarcoma
Mycosis fungoides
Retinoblastoma
Rhabdomyosarcoma
Wilms' tumor

While the above group of cancers is relatively limited, its emotional and social impact is greater than expected because of the development of these cancers predominantly in the young.

Variation and prolongation of life are regularly recorded with conventional therapies in prostate cancer, breast cancer, chronic lymphocytic leukemia, acute myeloblastic leukemia, ovarian cancer, neuroblastoma, and malignant insulinoma. This group of cancers is responsible for approximately twenty-five percent of cancer deaths; and in summary with the previous group, we have no more than one-third of lethal cancers showing a definitive response to chemotherapy.

The largest group of cancers left belong to cancer of the lungs, cancer of the gastrointestinal tract including pancreas and liver, cancer of the head and neck area, cancer of the uterine cervix, malignant melanoma, and various soft tissue sarcomas. This group is roughly responsible for two-thirds of all deaths from cancer, and palliation with various chemotherapeutic compounds is questionable. There is no data to support chemotherapy affecting the natural history of these diseases.

Essentially unsolved problems for further developments in the arts and science of chemotherapy demand greater insights into the kinetics of the cancer

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cell. The amount of time in the cell cycle wherein the cell is susceptible to the chemotherapeutic compound has to be better delineated. Also we need more insights into how chemotherapeutic compounds, both singly and when used in combination, remain viable in the blood stream. Developments of *in vitro* systems where we can expose isolated cancer cells to various drugs, such as we do successfully with identifying the appropriate antibiotic for bacterial infections, needs development. Currently the assays of tumor cells *in vitro* do not give us information that is of value in the treatment of a patient with a cancer. The relationship between chemotherapy and immunology needs more elucidation. It would now seem that one of the roles of chemotherapy is found with a rebound effect after the cessation of chemotherapy, which results in a more active and vigorous immunologic surveillance.

In the past six months there has been released by the FDA two new compounds, Bleomycin and Adriamycin. Bleomycin is used in combinations in treating various lymphomas and selected testicular cancers. However, to me its most exciting potential is in the treatment of epidermoid carcinoma. The chemotherapeutic regimen in the past utilizing Methotrexate locally with parenteral citrovorum factor to minimize system toxicity has shown minimal responses. Thirty percent response rates to squamous cell carcinoma of the head and neck are being reported from the administration of Bleomycin.² The incidence of the response rate is affected by the presence or absence of previous ionizing irradiation, and the drug has poor response in patients with head and neck cancer which has been radiated previously. The toxic effects of Bleomycin are similar to other radiomimetic drugs with mucositis, alopecia, anorexia, nausea, and vomiting. Peculiarly specific to Bleomycin is, however, pulmonary fibrosis. This is the most serious toxic effect with Bleomycin and has been recorded in approximately

ten percent of the treated patients. The toxicity of Bleomycin is dose-related, however, and when the total dose is kept under 400 units, complications are infrequent. We have encountered no serious complications in the treatment of some twenty-three patients with various types of epidermoid carcinoma during the past six months. I believe that Bleomycin is properly part of our clinical armamentarium. The instructions on the bottle are adequate and this drug has a real potential for reaching a large volume of patients which, heretofore, has had nothing of any promise.

Adriamycin is another recently FDA released drug and is very much a cousin of Bleomycin in being a cytotoxic antibiotic isolated from a strain of *Streptomyces peucetious* variant *caesius*. Adriamycin, unlike Bleomycin, seems to have an effect on a large diverse group of neoplasms. Like Bleomycin, it has a role to play in selected lymphomas. It seems to be also effective on soft tissue sarcomas.³ A radiomimetic effect has given it what should be a role in breast cancer. The Southwest Oncology Group has reported a fifty-five percent response rate with the patients receiving the recommended dose of 60 mg/m² every three weeks.⁴ Other cancers which have not shown marked response to chemotherapy such as transitional cell bladder cancer, bronchogenic lung cancer, non-epidermoid and thyroid carcinoma also have shown response rates to Adriamycin. Common denominators with Bleomycin in toxicity are alopecia, nausea, vomiting, stomatitis. Leukopenia is much more common with Adriamycin. Its major toxicity is on the heart, producing EKG abnormalities and a mild cardiopathy. Adriamycin, like Bleomycin, may find in the future its most effective role in combination with other agents. Such studies are now underway.

CONCLUSION

Chemotherapy with better screening techniques continues to present to the clinician new therapeutic tools. I think

CANCER TOPICS

it is most appropriate that Bleomycin and Adriamycin are now released for clinical use. They are powerful tools, and, of course, require attention to detail. I feel, however, their potential for palliation in the above mentioned cancers which heretofore have had no appropriate chemo-

therapeutic compounds justifies their more widespread use. Ongoing studies where these drugs are used in conjunction with others will be followed closely and reported when the evidence has been accumulated.

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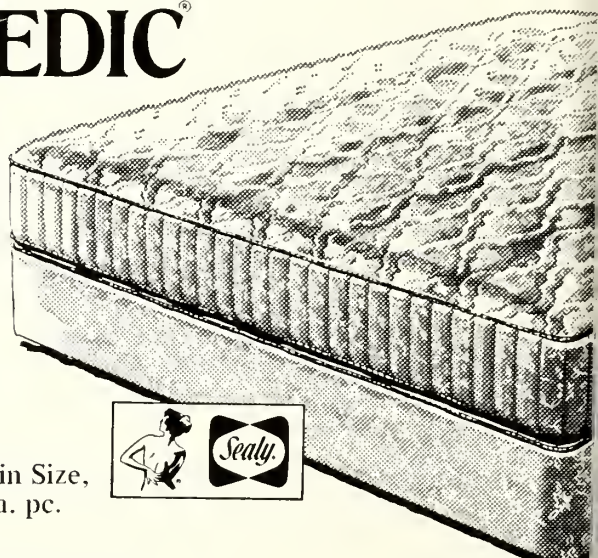
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FIRST AID TRAINING IS VITAL FOR EFFECTIVE EMERGENCY MEDICAL SERVICES

VINCE MOSELEY, M. D.*

Dr. George T. Wolff, as a member of the Commission on Health Care Services of The American Academy of Family Physicians, has recently pointed out the need for prompt first aid at the scene of an accident if we are to significantly reduce death and severely disabling injuries.

Death from accidental trauma is increasing yearly. All too often, death is as a result of improper management at the scene of the accident, and many deaths or permanently disabling injuries could have been prevented had persons immediately at hand had some knowledge of basic first aid.

Much is being done to improve emergency services in South Carolina and, throughout the U.S., ambulance vehicle requirements have been made more stringent, and so have the training of emergency personnel and their operational techniques. BUT—how often does a trained emergency technician, a registered nurse, or a doctor happen to be present as an accident occurs? Improvement in emergency services is vital, and steps being taken to upgrade them are laudatory, but to effectively decrease traumatic deaths from automobile and other accidents, the public needs to have training and knowledge of first aid, with clear guidelines for action to reinforce this knowledge when an accident occurs.

How can such information be furnished? A list of directions and advice should be furnished to home owners by insurance policy agencies, health departments, local medical societies and, also, be

*Charleston, S. C.

placed in every automobile for a start in the right direction. Spot TV and radio announcements to reinforce such a pamphlet, as a public service, is also a feasible approach. The first aid list could be automatically included in the Car Owner's Manual and kept in the car at all times for quick review.

To be effective, such lists and directions in first aid must be concise, clear, and should be written and illustrated in the simplest terms. Some of the main points which should be stressed:

First, seek skilled help as quickly as possible. A universal emergency telephone number would be most helpful.

Second, check on breathing and insure an airway. This is of the first priority in an unconscious patient. Instructions and illustrations for clearing the mouth, elevating the jaw, and bringing the tongue forward as well as the giving of mouth-to-mouth resuscitation are vital but with appropriate precautions about the head and neck movements when cervical spine fracture might be present, as in instances where head and neck injuries have been sustained.

Third, determine if the heart is beating by appropriate instructions as to closed chest cardiac compression, stressing the need for a firm flat surface when this maneuver is performed.

Fourth, determine if the person is bleeding with appropriate illustrations of how to apply pressure to bleeding points.

Fifth, if the patient is conscious, question about areas of pain, examine for

FIRST AID TRAINING

evidence that might suggest a fracture, and, if suspicious, splint. If the victim is not conscious, examine for deformities that would suggest a fracture and, if found, splint before moving. The usefulness of splints, made from newspapers, magazines, towels, or pillows to steady but with bindings not so tight as to be of danger to the circulation, should be stressed to avoid added trauma from movement.

Sixth, keep the patient covered and warm until help arrives to aid in proper transport to a medical facility.

Appropriate first aid while waiting for ambulance or other trained personnel to arrive will frequently mean the difference between life and death. Notification of need for aid to trained services personnel is prime and should not be postponed for purpose of description or identification.

How can the American people be ed-

ucated in this manner? Many organizations are already doing a great deal to train people, such as the Girl and Boy Scouts, the Heart Association and its volunteer groups, and the American Red Cross. Many industries, also, are training their employees. Much of the public, however, is not exposed to such training, or because of disuse, forgets. Such training needs to be refreshed. Physicians should use their influence to stimulate such training opportunities and programs.

Because of the increasing lethal outcome of automobile accidents, first aid should be included as part of a driver's education program, and questions concerning first aid procedures might also be included on the driver's license test. Better trained emergency technicians, nurses, and doctors, will not be enough to do the job or make for truly significant reductions in accidental deaths.

Vince Moseley, M.D.

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ACCREDITED BY THE J. C. A. H.

President's Pages



Dear Fellow Physicians of South Carolina:

Since our last letter in June, activities have been continuing to move at a very rapid pace. Council has approved, and letters have been sent to some 250 members of our Association to serve on the active committees for 1975-76. In these letters, we have requested that the members participate fully in the committee's activities and attend the meetings, and contribute to the business at hand. Of course, every member of every committee has to be a member of the South Carolina Medical Association to serve, and those men who were found not to have renewed their membership have been requested to do so.

We, the doctors of South Carolina, can prove to the public and to the nation, that "the South will rise again" and do all in our power to enhance the doctors' image in the public's eye. We recognize that there are problems, but we plan to face the problems and do something about them. This requires and necessitates that every physician, three thousand (3,000) to be exact, no matter how insignificant or important that he may feel personally, must do something, no matter how small, to help the medical profession in this time of great need. The task at hand is so great and so many problems beset us that all need to put their shoulders to the wheel. The officers and members of Council can not do the job alone, and I appeal to each of you as practicing physicians in South Carolina to join the S. C. Medical Association; let's unite and move forward as a team, with each contributing to solve the many perplexing issues facing us.

In the last two months, the Medical Liability Insurance problem has been occupying much of our time. At the present time, the Joint Underwriting Association has been activated and is accepting applications for liability coverage from the physicians of the State. The Liability Committee of the S. C. Medical Association recommended Dr. John Sutton and Dr. Kilgore to be a member of the Governing Board of this JUA. The Governor appointed a Dentist, Dr. Huffman of Greenville, and Dr. John Sutton of Columbia, to serve on this Board. They have had a meeting, and Dr. Sutton is actively working to represent the interests of the public, and the medical profession, in this Association.

We expect that there will shortly be appointed the Committee to study the malpractice problem in South Carolina. The Senate has appointed its three members, and I believe that the House will do so shortly. Dr. Kilgore and I will probably be appointed by the Governor to represent the medical profession on this Study Committee. I assure you that we will do our utmost to work with the gentlemen of the Committee to arrive at the best possible solution, through the legislative process, for every citizen of South Carolina.

Dr. Edmund Taylor, Dr. Lamar Priester, and myself had a one and a half hour conference recently on the emergency medical care for South Carolina, and we expect the Emergency Medical Care Committee of the S. C. Medical Association to be actively involved in working throughout the State to offer the finest emergency medical service possible. Letters have been written to Presidents of all specialty societies to appoint one of their members to the Legislative Committee. Each medical district has had a member appointed to the Legislative Committee, as well as the seven appointed members by Council. This will total thirty-four members of the Legislative Committee, with seven members of the Professional Liability Committee, and seven members of the Public

Relations Committee. I am hopeful that, in the very near future, these approximately fifty doctors can be called to a joint meeting to outline the necessary steps for the S. C. Medical Association to follow in presenting our program on the Medical Liability Insurance problem to the citizens of South Carolina and, particularly, to the Legislators so that positive action can come out of the General Assembly in 1976.

I would like to urge as many members and officers of local medical societies as possible to attend the Speaker's forum at the Mills Hyatt House in Charleston on August 15, 16, and 17, as outlined in the publicity previously sent to the membership.

All men of courage and conviction did not die two thousand years ago. All heroic Americans did not live in 1776. Many of them are members of our Association. Let's lose ourselves in the challenge to think enthusiastically about the South Carolina Medical Association, and about our profession, and the great responsibilities and privileges we enjoy today as fellow citizens of these United States. Notwithstanding all the news we hear about the world today, we know the world is getting better and our blessings are continuing to increase and, thanks to medical research, many are living to a much riper old age today. Let's lose ourselves this year in the oldtime religion of "giving all we have to do the job we must do." Let's get iron in our blood and bone in our backs, and strive harder than ever to stand up for the high ideals and ethics of our profession to give ever increasing quality medical care to the citizens of our great State of South Carolina.

Sincerely,
C. Tucker Weston, M. D.
President
South Carolina Medical Association

Randomycin[®]

(methacycline HCl)

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**

Usage in pregnancy. (See above **WARNINGS** about use during tooth development.) Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate observed in premature given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms) anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea. In uncomplicated gonorrhea, when penicillin is contraindicated, "Randomycin" (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule: 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of "Randomycin" (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia: 900 mg daily for six days.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

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* WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Indications: *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



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Editorials

Medicine, Russia, Shock, and the Future

Bill Hunter's excellent thoughts enunciated in "Medicine's 'Future Shock'" bring a refreshing new consideration into medicine's socioenomic turmoil — the patient. The extensive dialogues we have seen recently have concerned the "providers," the "consumers," peers and peer reviews, liability cases, plaintiffs, defendants, medical schools, medical students, etc., etc., but rarely do we hear about *patients*. Hunter presents a real problem that must be dealt with realistically in the near future.

It is interesting to compare Hunter's concerns with Warren Irvin's view of Russian medicine. Their Communist government apparently has found a way to provide sufficient medical personnel to fulfill their needs. It is difficult to believe that the highest quality people can be attracted to medicine in Russia when factory workers earn two to three times as much as doctors unless they have found some motivation other than earning family keep.

Professor Jay W. Forrester of M.I.T. is Director and spokesman for Systems Dynamic Group, a team of professors and doctoral students who have for the past three years been developing a model of social and economic behavior in the United States. It will have a 250-year span, from 1850 through the year 2100. This effort has attracted worldwide attention and has already allowed Forrester to reach some conclusions about the future. Greatly simplified, Forrester's ideas are that growth is a temporary process. This is just as true with our society as with our body. Growth always runs its course.

Growth produces its own termination. Any growth that repeatedly doubles will at some time overwhelm its host environment. Given the pressures, it will be impossible for the United States to maintain its present quality of life. The country can no longer afford to squander its natural resources, extol the virtues of size, sustain its standard of living and plan haphazardly for tomorrow without paying the price of "future shock." Forrester believes time is short to make decisions to reverse these trends. The next decade will be critical. We must face the alternatives.

Under Forrester's thesis, as the growth phase of our civilization gives way to the phase of stability, we must make choices between continued population increases and quality of life. According to him, we can't have both. Either choice will have similar implications on the practice of medicine in the future.

Let me illustrate with a few simple examples of medical choices. We know that angina can be reduced and perhaps life extended by coronary by-pass surgery. This costs \$5,000 to \$6,000 in direct medical care costs plus a 6-8 week disability for the patient. Or total hip replacement can restore function to a painful disabled joint at a medical cost of \$3,000 to \$4,000 and 6-8 weeks of disability for the patient. As medical economics undergoes the transition from growth to stability, it will be impossible to provide everyone with precordial pain or hip pain the very expensive operation which will increase the quality of his life.

The hard driving executive who has chest pains hurrying from the Board Room to meet with the Union Grievance Committee and the mother of 8 children who has to stop several times on the way to buy food stamps with her relief money because of pains in the chest, and the many others cannot all be provided with their operations. The plumber who no longer can do any upstairs work and soon will have to stop all work because of pain in his hip and the old man in the rest home who has to hobble so slowly and painfully as he is gently led to his supper and all

the rest like them cannot be provided with the hip surgery that would relieve them. In the phase of stability, there just are not enough resources. So what do we do?

Under the capitalistic system, those that can afford it get it, those that can't, don't. Under the socialist system, there is help available to everybody, but it seems very mediocre. There must be a better way. And we must find it soon. Perhaps Bill Hunter has found it. I don't think the Russians have.

EEK

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Indeed, many a driver who deserves a Rolls-Royce, and could indeed afford one, proceeds instead to buy another luxury car.

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Silver Shadow owner is not forced by economics to trade in his car just when he's beginning to know it well.

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Book Reviews

CARDIAC ARREST AND RESUSCITATION by Hugh E. Stephenson, Jr., M. D., FACS, AB, BS., 4th Edition, The C. V. Mosby Co. St. Louis. 1974. Pp. 998. Price \$44.50.

Hugh Stephenson's book, now in its 4th edition, is a classic in its field. It is an excellent source book for any physician interested in this special area. A large number of authoritative contributors cover every aspect of cardiac arrest and resuscitation exhaustively, and an extensive bibliography is appended. In addition, the complete standards for cardiopulmonary resuscitation and emergency cardiac care developed at the National Conference held in Washington, D. C., in May 1973, are made a part of the text. A minor flaw is the fact that over-lapping of certain material appears in articles by various contributors, which could have been eliminated by somewhat more rigid editing. However, the book represents the definitive work in its field and should be in every library as well as appeal to many persons interested in this special area.

TREATMENT OF CARDIAC EMERGENCIES by Emanuel Goldberger, M. D., FACP., 1st Edition, The C. V. Mosby Co. St. Louis. 1974. Pp. 355. N. P.

Treatment of Cardiac Emergencies by Dr. Goldberger is a paper-back handbook, rather than an exhaustive treatise. In general, it is well written, but dogmatic (not necessarily a fault in text about emergency treatment). However, the section of cardiac arrest is not written in accord with the latest (1973) standards as described above, and some ideas, i.e., employing leg elevation and precordial thump in all CPR emergencies, do not meet the current standards for management. Also it is unfortunate that a new drug such as

diazoxide is not mentioned under drugs for cardiac emergencies. The book is aimed more at the general practicing physician rather than the specialized cardiologist. Despite these minor faults, the book is a very useful one for those involved in the management of cardiac emergencies.

Ambrose G. Hampton, Jr., M. D.

IS IT WELL WITH THE CHILD? A Parents Guide to Raising Mentally Handicapped Children by Susan Strauss. Doubleday and Co. Inc. Garden City, New York. 1975. Pp. 152, price \$7.95.

To any parent with a child for whom problems are foreseen at birth or early childhood, this book will certainly provide help, help as comfort that there are many other people who have similar problems and help in making the very important decision about handling the problems that come with having a mentally handicapped child.

Susan Strauss tells of her experience with her child, Michael, from his very "normal" birth to the placement of Michael in a residential school. As in many cases, when Michael was born his parents were assured he was a normal and healthy baby. Susan Strauss goes into her feelings as Michael grew and as she realized he was not normal and was not developing like his older brother had developed.

Michael was first evaluated at age four. His tests are described as are the fears and uncertainties of his parents when they were told he was "autistic."

After his diagnosis his parents began the task of finding a school suitable for Michael, first, a day school and then, after problems within the family, a residential school.

In her suggestions for selecting a residential school, she mentions looking to see if there is a place for the child's toothbrush and a place for personal items, something that could be very important to a child but a parent desperately trying to place his child might overlook.

Ms. Strauss not only describes the autistic child but also other types of mentally handicapped children, from the severely brain damaged who must be fed, to the ones who can be taught simple academics. She includes conferences with parents of

these children and the problems they have faced.

Although the realism of having a mentally handicapped child is sometimes never really faced by a parent, this book can help many parents in facing the problems and the painful placing of the child in a school.

Mary M. Branyan
Special Education Teacher
Brennen Elementary School
Columbia, S. C.

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New SCMA President, C. Tucker Weston, M.D., presents memento to AMA Trustee Richard Palmer, M.D., for his remarks to Council

Dr. Weston Elected



Donald G. Kilgore, Jr., M.D., presents plaque to Michael Holmes, M.D., for nine years as seventh district Councilor



Harold P. Hope, M.D., receives plaque commemorating nine years Council service and Past Presidency



William C. Cantey, M.D., is recipient of Community Service Award



SCMA thanks outgoing President Donald G. Kilgore, Jr., M.D.



Mrs. Wayne C. Brady watches as Mrs. Norman H. Gardner of the AMA Auxiliary pins her Presidential replacement, Mrs. John M. Shingler, Jr.



Dr. Weston gives views before the House of Delegates

South Carolina doctors installed C. Tucker Weston, M.D., a Columbia orthopedic surgeon, to be the 1975-76 President of SCMA at its Annual Meeting held May 4-7 at Myrtle Beach. Dr. Weston succeeds Donald G. Kilgore, Jr., M.D., of Greenville.

Dr. Weston previously served SCMA as Speaker of the House of Delegates, and he has served for four years as an alternate

Palmer stated that the AMA staff had been trimmed back and that other costs have been reduced, but that an AMA dues increase is necessary. He pointed to recent law suits against HEW to protect private physicians against governmental encroachment as the primary cost problem.

The professional liability insurance problems were the major points of discussion, but other important events were

President at SCMA Convention

delegate to the AMA. The new SCMA President served in many leadership roles and was President of Sertoma International in 1959-1960. He has received several awards and life memberships, and his alma mater, The Citadel, bestowed upon him an honorary degree.

Also elected at the SCMA Convention were: John D. Gilland, M.D., of Conway, as President-Elect; and Michael Holmes, M.D., of Kingstree, as Vice President. Re-elected were: D. Strother Pope, M.D., of Columbia, as Secretary; and J. Ernest Lathem, M.D., of Greenville, as Treasurer.

The meeting was highlighted by the appearances of three special guests. South Carolina's Governor James B. Edwards was guest speaker at the SOCPAC luncheon urging the members to get involved and to back qualified candidates. Neal R. Peirce, author and commentator from Washington, spoke at the annual banquet.

Richard E. Palmer, M.D., Chairman of the AMA Board of Trustees, appeared before the SCMA Council and the House of Delegates to give the AMA report. Dr.

also covered. Reference committees met to make recommendations to the House of Delegates for guidelines and goals for the coming year.

Three physicians received awards for outstanding service. Dr. William C. Cante, of Columbia, received the coveted Physician's Award for Community Service which was contributed by A. H. Robins. Dr. Harold P. Hope, of Union, and Dr. Michael Holmes, of Kingstree, received plaques commemorating their nine years of service on the Council of SCMA. Dr. Hope is also a Past President.

The Woman's Auxiliary to the SCMA held their meetings correspondingly with their husbands. They elected Mrs. John M. Shingler, Jr., of Spartanburg, to be the new President succeeding Mrs. Wayne C. Brady, of Greenville. The ladies had as their special guest Mrs. Norman H. Gardner, the First Vice President of the AMA Auxiliary. Mrs. Brady appeared before the SCMA Council and the ladies reported their activities to the House of Delegates.

Doctor, Do You Extend Credit?

If you, as a physician, accept payment for your services in installments, you could be required to register with the South Carolina Department of Consumer Affairs.

The S. C. Consumer Protection Code, effective January 1, 1975, states that if a professional:

1. extends credit and collects a service charge, *or*
2. accepts payment of bills in 4 or more installments, he is granting credit within the purview of the Consumer Protection Code. Those extending such credit must file notification with the Department of Consumer Affairs and pay a \$50 registration fee.

The filing deadline for such notification was January 31, 1975; however, as many professionals are unaware that their business practices may be covered by the Code, the Department is willing to accept late filing. Notification may be made on the standard notification form or in a letter. This notification should include the name in which business is transacted, the name of the individual or organization filing the notification, and the address of the principal office from which business is conducted. If business is conducted at more than one office, the additional addresses should be included. The letter should also include the statement, "the information contained above is true and correct to the best of my knowledge and belief," and have the signature, name, and title of the person filing the notification.

If you allow credit of either type mentioned above, or have other questions regarding the Consumer Protection Code, contact the S. C. Department of Consumer Affairs at P. O. Box 11739, 600 Columbia Bldg., Columbia, S. C. 29211, or telephone 758-2040.



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Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

Overdosage may cause a curare-like action, with loss of voluntary muscle control.

For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

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Precautions: Since varying degrees of urinary hesitancy may be evidenced by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

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Pro-Banthine is provided in several different dosage forms which will meet virtually any clinical need. It is just as versatile in filling patient needs, among which are:

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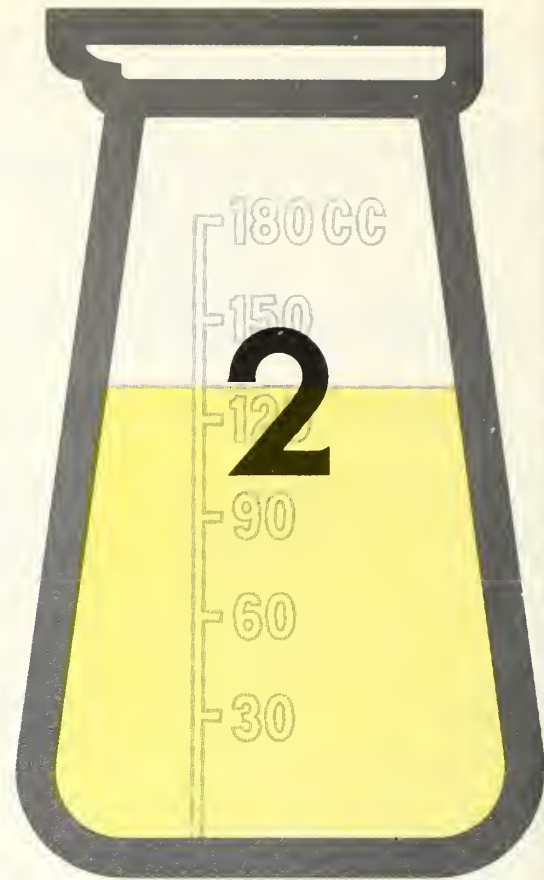
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Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprotrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d. depending on severity of infection.

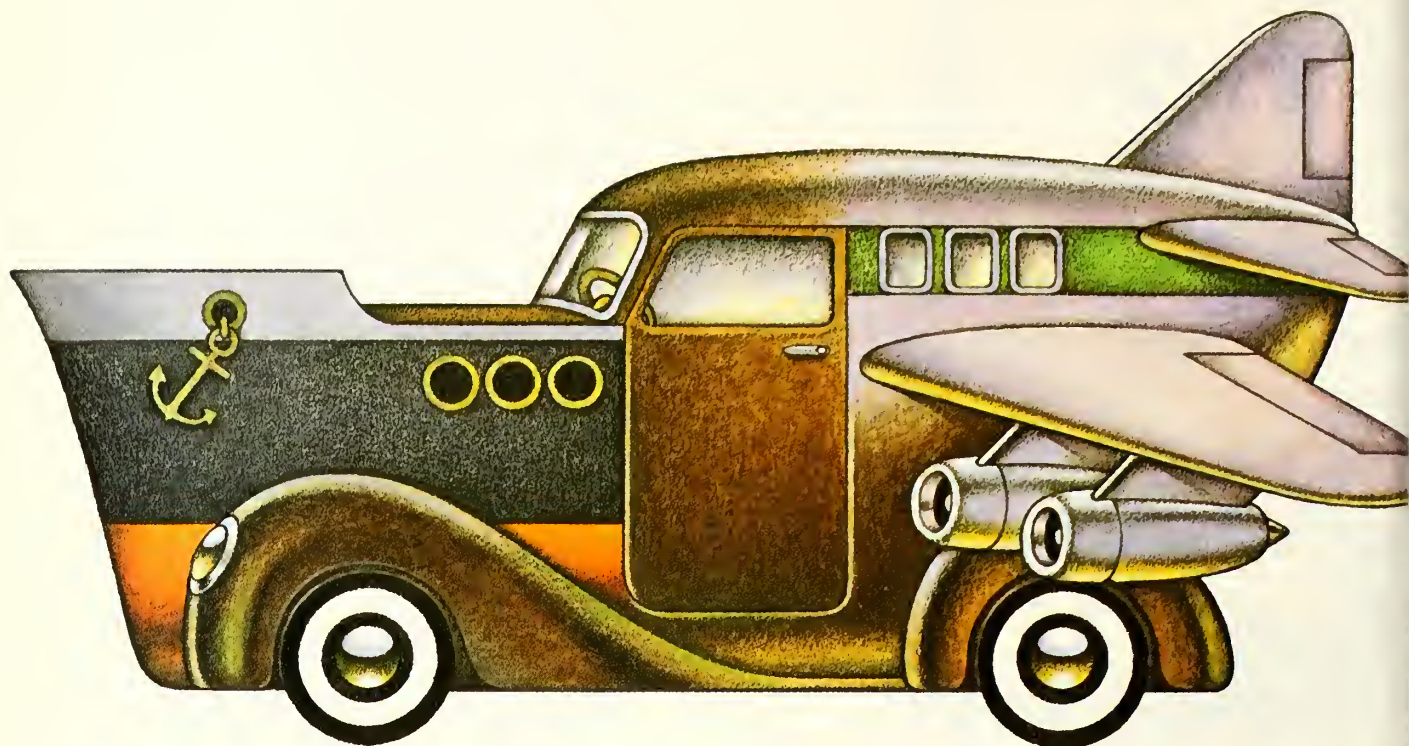
Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs b.i.d. Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.



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not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

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Rocky Mountain Spotted Fever Advisory

—By the S. C. Department of Health and Environmental Control—

This is the time of year to increase the index of suspicion for Rocky Mountain Spotted Fever, also called tick typhus or American tick-borne spotted fever.

The South Carolina Department of Health and Environmental Control (DHEC) has observed a significant increase in the incidence of Rocky Mountain Spotted Fever in the state during the past 6 years. The first cases are usually reported in early May, with the peak number of cases coming in August.

Physicians are asked to be on the alert for febrile illnesses which follow tick bites or exposure in tick-infested areas. When Rocky Mountain Spotted Fever is suspected, serological confirmation is available from the Department of Health and Environmental Control Laboratory at 2600 Bull Street in Columbia. At least 2 serum specimens, collected 2 weeks apart, should be submitted to the State Laboratory in order to determine a rise in antibody titer. All cases should be reported to the DHEC Division of Epidemiology via the local county health department.

Severe headache, listlessness, myalgia, sudden chill, rapid rise in temperature and rash are characteristic symptoms of the disease and when a history of exposure to ticks is also present, the diagnosis is suggested. Symptoms may occur from two to twelve days after a person has been bitten by an infected tick. The distinctive rash usually appears on the extremities during the third day of the disease; early rash may resemble measles or other rash illnesses.

When diagnosed early, Rocky Mountain Spotted Fever can be treated successfully by the tetracycline drugs or chloramphenicol. Vaccines are available, but due to the questionable effectiveness of current vaccines and the low risk of contracting the disease, the vaccine is recommended only for special situations such as laboratory personnel working with *Rickettsia rick-*

settsii and persons whose occupations result in repeated exposure to ticks in endemic areas.

Only live ticks that are removed from human beings should be mailed to the following address to determine if the tick is infected with a rickettsial organism.

Division of Vector Control
South Carolina Department of Health
and Environmental Control
2600 Bull Street
Columbia, South Carolina 29201

Due to the large volume of ticks submitted, we cannot examine those removed from animals or the environment.

It is requested that all live ticks submitted be placed in a medicine vial containing a small strip of paper towel moistened with *one drop* of water. Attached information should include date, locality, host, collector and telephone number of physician or patient. The sender can expect a telephone reply if tests are positive.

If a positive tick was removed from a patient whose signs and symptoms are compatible with a diagnosis of Rocky Mountain Spotted Fever, treatment can be initiated.

Fifty-five cases of Rocky Mountain Spotted Fever were reported in South Carolina during 1974, including five fatal cases. The fatalities were two young girls, ages two and five; a 49-year-old woman, and a couple in their forties. More than three-fourths of the cases reported occurred in the Piedmont or above the fall line.

The American dog tick, *Dermacentor variabilis*, is the most prevalent tick in South Carolina and a potential carrier of tick-borne typhus. Not all ticks are infected. Even in heavily-infested areas, only about one tick in twenty is infective and, therefore, able to transmit Rocky Mountain Spotted Fever.

GENERAL PRACTICE REVIEW COURSE

September 7-13, 1975

The Board Examinations of the American Academy of Family Physicians will be given November 1-2, 1975. Therefore, The Division of Continuing Education of the Medical University of South Carolina will offer again the Sixth Annual Family Practice Refresher Course for those who may have missed it in February or who may wish to attend again. Thirty-eight and one-half (38½) AAFP credit hours will be given for attendance at this course. Lectures will be presented at the Mills Hyatt House Hotel with visits to various units of the Medical University complex for tours and demonstrations. The dates for this repeat course are September 7-13, 1975.

Registration is open now through Au-

gust 25, 1975. Enrollment is limited to 75, and tuition is \$150.00 payable in advance on or before September 7, 1975. A block of rooms is being held at the Mills Hyatt House Hotel at special convention rates. The Social Hour and Banquet on Wednesday evening is included in this fee. Wives are cordially invited.

A registration desk will be open from 6:30 to 8:30 p.m., Sunday evening, September 7, in the Middleton Room on the first floor of the Mills Hyatt House Hotel for the convenience of those participants wishing to complete their registration at that time. Final registration will be in the pre-assembly area at 8:00 a.m., Monday, September 8.

Please detach and return

REGISTRATION

GENERAL PRACTICE REVIEW COURSE

September 7-13, 1975

NAME _____ TELEPHONE NUMBER _____

ADDRESS _____ ZIP CODE _____

_____ Enclosed is \$150.00 tuition fee for General Practice Review Course

_____ Please send me hotel reservation card for Mills Hyatt House

_____ I plan to attend Social Hour and Banquet Wednesday evening

_____ My wife will also attend Social Hour and Banquet

Please make check payable to: Division of Continuing Education, MUSC, and mail to Dr. Vince Moseley, Director, Division of Continuing Education, Medical University of South Carolina, 80 Barre Street, Charleston, S. C. 29401.

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Mrs. Andrew J. Whitaker, 6106 Crabtree Rd., Columbia, S. C. 29206

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- Often effective when reassurance and counseling are insufficient.
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Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

Precautions:

ORAL: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six.

INJECTABLE: Keep patients under observation, preferably in bed, up to three hours after initial injection; forbid ambulatory patients to operate vehicle following injection; do not administer to patients in shock or comatose states; use reduced dosage (usually 25 to 50 mg) for the elderly or debilitated and for children age twelve or older.

ORAL AND INJECTABLE: Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating compounds such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual



precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduc-

tion; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

With the injectable form, isolated instances of hypotension, tachycardia and blurred vision have been reported; also hypotension associated with spinal anesthesia, and pain following I.M. injection.

Usual Daily Dosage: Individualize for maximum beneficial effects. **Oral: Adults:** Mild and moderate anxiety and tension, 5 or 10 mg t.i.d. or q.i.d.; severe states, 20 or 25 mg t.i.d. or q.i.d. **Geriatric patients:** 5 mg b.i.d. to q.i.d. (See Precautions.)

For Parenteral Administration: Should be individualized according to diagnosis and response. While 300 mg may be given during a 6-hour period, do not exceed this dose in any 24-hour period. To control acute conditions rapidly, the usual initial adult dose is 50 to 100 mg I.M. or I.V. Subsequent treatment, if necessary, may be given orally. (See Precautions.)

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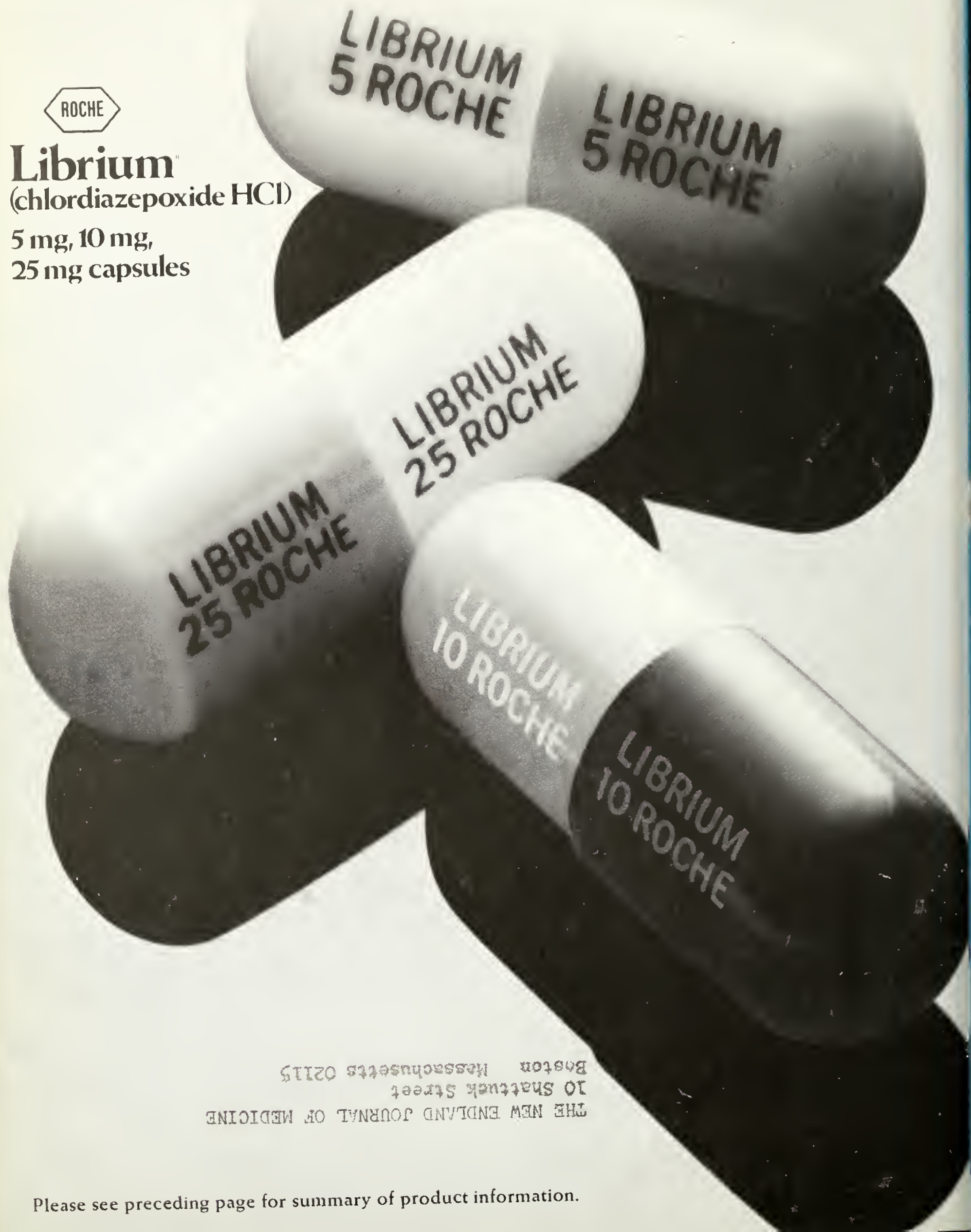
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VOLUME 71

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NUMBER 8

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Both often



- Predominant psychoneurotic anxiety

- Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor

neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

SEP 8 1975

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent

in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



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(diazepam)
2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.


Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



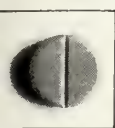
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† If the patient is not cured three weeks after treatment, a second course of treatment is advised.

highly effective

	Mean Cure Rate (Range)	Mean Egg Reduction (Range)	No. Patients	No. Studies
Whipworm (<i>Trichuris</i>)	68% (61-75%)	93% (70-99%)	211	(5)
Roundworm (<i>Ascaris</i>)	98% (91-100%)	99.7% (99.5-100%)	101	(2)
Hookworm	96% (—)	99.9% (—)	23	(3)
Pinworm (<i>Enterobius</i>)	95% (90-100%)	— — —	524	(7)

simplicity of administration

patients can take the tablet at any time.
It can be chewed, swallowed or crushed and mixed with food. No messy liquids to pour.

not a dye new Vermox® (mebendazole) chewable tablets will not stain clothes, teeth, feces, toilet bowls, etc.

convenient neither laxatives nor special diet required. Therapy does not interfere with daily activities.

well tolerated

transient symptoms of abdominal pain and diarrhea have occurred
in cases of massive infection and expulsion of worms.

Vermox has not been extensively studied in children under 2 years of age, and thus, the relative benefit/risk
should be considered before treating these children. Vermox is contraindicated in
pregnant women. (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Indications Vermox® (mebendazole) is indicated for the treatment of
Trichuris trichiura (whipworm), *Enterobius vermicularis* (pinworm),
Ascaris lumbricoides (roundworm), *Ancylostoma duodenale* (common
hookworm), *Necator americanus* (American hookworm) in single or
mixed infections.

Efficacy varies in function of such factors as pre-existing diarrhea and
gastrointestinal transit time, degree of infection and helminth strains.
Efficacy rates derived from various studies are shown in the table below:

	Trichuris	Ascaris	Hookworm	Pinworm
cure rates mean (range)	68% (61-75%)	98% (91-100%)	96% —	95% (90-100%)
egg reduction mean (range)	93% (70-99%)	99.7% (99.5-100%)	99.9% —	— —

Contraindications Vermox is contraindicated in pregnant women
(see: Pregnancy Precautions) and in persons who have shown hyper-
sensitivity to the drug.

*TRADEMARK

Precautions **PREGNANCY:** Vermox has shown embryotoxic and terato-
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Adverse reactions Transient symptoms of abdominal pain and diar-
rhea have occurred in cases of massive infection and expulsion of worms.

Dosage and administration The same dosage schedule applies to
children and adults.

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secutive days. For control of enterobiasis, a single tablet of Vermox
is given.

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AUGUST, 1975 — VOL. 71, NO. 8

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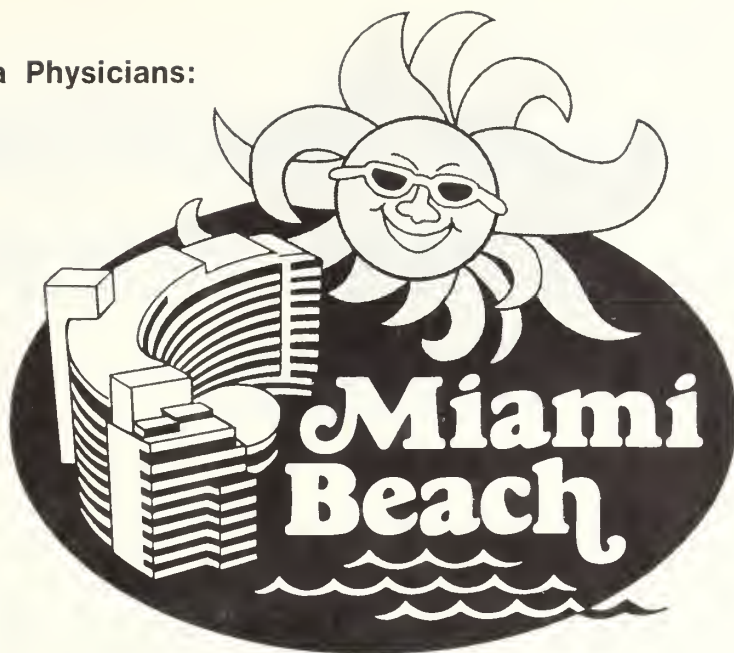
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THE JOURNAL

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SOUTH CAROLINA'S PERINATAL HEALTH

HENRY C. HEINS, Jr., M.D., M.P.H.*

Someone has said "a nation's health is its wealth." If this is true concerning South Carolina's perinatal health, we are flat broke or bankrupt!!

As most of you realize, South Carolina is and has been third from the bottom in the United States' perinatal mortality. Only a few percentage points separate the lower most ten states in this country in perinatal mortality. All of these states are in the southeastern section of our country and share similar problems.

Fetal, neonatal, and perinatal rates are indicators of community health. Although perinatal mortality is associated more closely with events immediately surrounding births, numerous other factors, such as poor home environment, lack of education, and low socio-economic status, must be considered. No report derived solely from birth and death certificates can bring to light all factors affecting mortality. In evaluating services, the social, cultural, and economic characteristics of the population served carry considerable weight. However, these factors are disregarded when politicians lay the blame at the door of the physician.

Perinatal deaths, both fetal and neonatal, are usually reported by county of occurrence or county of residence. Now

for the first time, we have them reported by hospital. Since this perinatal program has been programmed for the computer, it is possible to do a ranking of maternity services by perinatal mortality annually.

Sixty-six of sixty-eight hospitals with active maternity services in 1972 (97%) responded to a perinatal services questionnaire. The 25 item questionnaire reveals some interesting data about the delivery of perinatal health care in South Carolina. This study was cross-validated by an analysis of fetal and neonatal deaths from a review of fetal death certificates and matched birth and death certificates for the year 1972.

The hospitals were classified into six groups according to the size of maternity service. More than one-half of the maternity services in South Carolina have less than 500 deliveries per year. Only 20 per cent of South Carolina's births occur in these small services, but significantly, it is here that more than 30 per cent of the fetal deaths and 50 per cent of the maternal deaths occur (figure I).

Utilization of delivery rooms and maternity beds does not reach the South Carolina mean until more than 500 births occur on a service. The mean of less than 0.9 delivery per day shows very poor utilization of facilities (figures II & III).

It must be emphasized that the problem is mostly one of medical indigency. The majority of obstetrical patients in South

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PERINATAL HEALTH

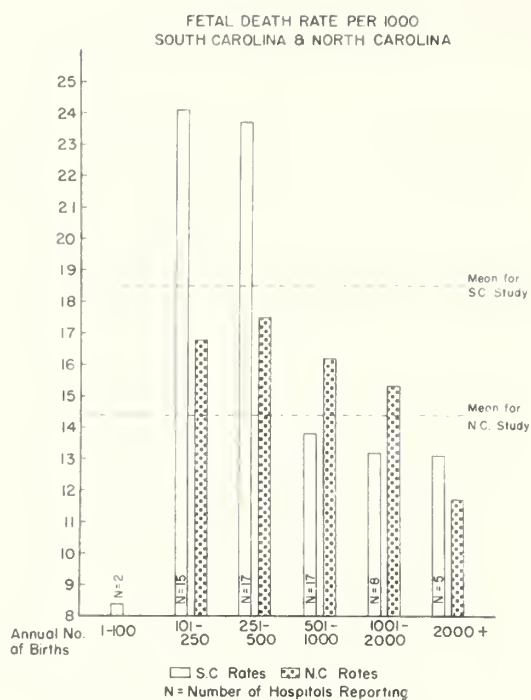


Figure 1

Carolina get good obstetrical care as private patients when they can afford it. And, it must be emphasized that the possible solution to this problem will be a plan that centers around the early identification of the high-risk patient. If we are successful with early identification of the high-risk patient in a regionalized concept, care of the low-risk patient will not be a problem.

The plan I wish to outline is not unique as many states have begun development of regionalization of perinatal health facilities. How is such a regionalization of perinatal services developed?

1. The system has to be completely voluntary.
2. Time has to be spent in various community hospitals in order to gain an adequate understanding of the local problems and how they are dealt with. Absentia review of data from hospitals has been shown to give a poor index of health care quality. Most of the prob-

lems of regionalization are local and solutions must relate to these local problems.

3. The local area has to be receptive to changing patterns of health care.
4. Any suggested change in the pattern of health care has to be tested in a comparable setting; what works in a university setting may have no relevance to what works in a rural-based center.
5. Local manpower and other resources have to be utilized even if this means a longer period of "on the job training." Awaiting the availability of highly trained people, such as perinatologists, takes too long a period of time.
6. A back-up resource has to be easily acceptable and available to developing centers for consultation and support.
7. Any approach to the changing of health care patterns has to be acceptable to the consumer of health. The big plan is worthless if the recipient of the plan is not supportive.

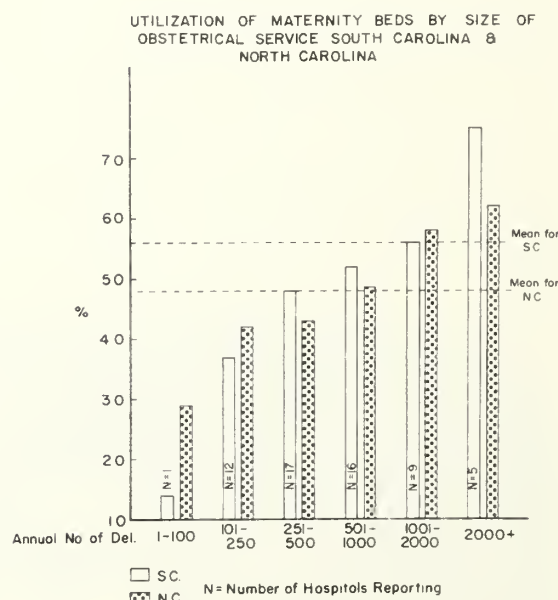


Figure 1

PERINATAL HEALTH

The proposal to regionalize perinatal care is intended to provide resources for the practicing physician and make available consultation services and medical facilities for any complexity in maternity and infant care in our state. The proposal is not intended to restrain or dictate medical practice. The responsibility of whom to hospitalize and where to hospitalize must remain within the province of the individual physician. Any such plan cannot succeed without the complete cooperation of the physicians involved.

Under such a plan, three hospital levels of care would be identified, each with certain characteristics of facilities, equipment and personnel. The three levels of hospitals recommended are:

Level I: Community hospitals (20-25) would deliver normal obstetrical and neonatal care.

Level II: District hospitals (10-12) would deal with most of the obstetric and pediatric problems.

Level III: Regional hospitals (3) would

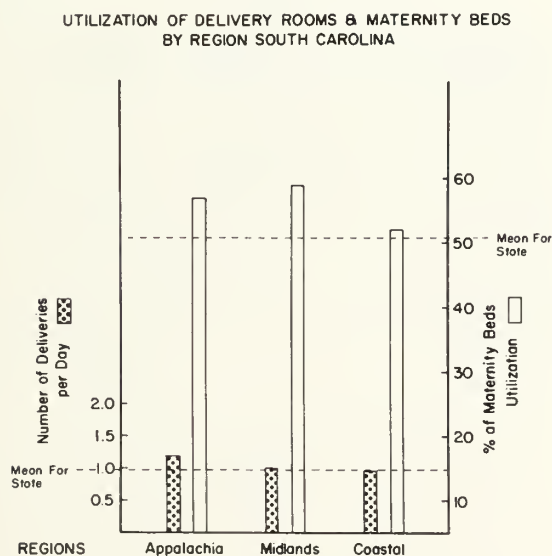


Figure 111

OBSTETRIC PATIENTS - HIGH RISK SCORE SHEET

ASSIGN HIGH RISK IF +5 OR GREATER SCORE:

- I. Socio-economic (+1 for any factor)
Age - less than 18 or greater than 34. _____
Parity - 0 or greater than 4. _____
Marital status - unwed. _____
Educational status - less than 12 years. _____
- II. Nutritional (+2 for any factor)
HB - less than 10 grams. _____
UN/TN Ratio - less than 60. _____
Height - less than 60 inches. _____
Weight - less than 100 lbs. or greater than 200 lbs. _____
- III. Past Pregnancy Performance (+3 for any factor)
Difficult labor - prolonged labor. _____
Damaged infant. _____
Congenital major anomaly. _____
Previous cesarean section. _____
- IV. Past Pregnancy Outcome (+4 for any factor)
Fetal death. _____
Neonatal death. _____
Low birth weight (less than 5½ lbs.) _____
3 + consecutive abortions. _____
- V. Medical or obstetric complication, present pregnancy
(+5 for this factor). _____

HIGH RISK SCORE

Indication for high risk care &
plan for care (outline):

Ultrasonic Laminography:

Date	♂ Wks.	BPD	Gest., Age
------	--------	-----	------------

2010-2011	2011-2012	2012-2013	2013-2014
2014-2015	2015-2016	2016-2017	2017-2018

3/0 - Online Condition

L/S & Other Studies.

	Value
--	-------

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Figure 1V

serve as centers for the care of the most complicated cases. These centers (Greenville, Columbia, and Charleston) should have a total commitment to continuing perinatal education in their regions.

After some two years of study, a National Task Force (made up of The American College of Obstetrics & Gynecology, The American Academy of Pediatrics, The National Organization of Family Practitioners, and The American Medical Association, with The National Foundation-March of Dimes (acting as secretariat) has evolved specific criteria which establish a certification mechanism whereby a hospital is designated as Level I, II, or III perinatal care hospital.

PERINATAL HEALTH

One important facet of the plan, I believe, is the development and implementation of a data collection system which can detect high-risk patients while they are still at risk and which can delineate areas of professional and/or consumer educational inadequacy (figure IV). As far as data collection is concerned, standard definitions, standard forms, etc., are mandatory for quality care, as distasteful as they may be. There are developing computerized perinatal records which will require less record keeping time for the physician, therefore, allowing more time to be spent with his patients.

Hospital administrators will take a dim view, most likely, of the expensive equipment needed in a perinatal center, since the obstetrical service is usually a "loss leader" in most hospitals. This may be a factor in consolidation of small obstetrical services or pooling of resources to acquire monitoring equipment (figure V).

Perinatal mortality is just the tip of the "iceberg." Similar numbers of infants with neurologic deficits are important parts of the problem. It is very difficult to estimate the cost of reproductive casualties, such as patients with cerebral palsy and mental retardation.

It should be emphasized that the perinatal center represents a great educational resource. The regionalized perinatal concept is not a threat to the private practitioner who is invited and encouraged to use the premises for his high-risk patients. Both levels II and III will have to have "open staff" privileges for physicians doing obstetrics.

Although it is obvious that this plan is primarily directed to the medically indigent patients, benefits in perinatal care will certainly be derived by the private sector.

Finally, since this concept is very expensive to implement, surely public funds will have to underwrite the efforts to some degree. The Department of Health and Environmental Control will have to

take a leadership role in arranging this type of care for the medically indigent patient.

SUMMARY

- A. Perinatal mortality and morbidity in South Carolina are too high.
- B. The low socio-economic status of many South Carolinians contributes to this problem.
- C. Perinatal health care services are inconsistent in planning, organization, and delivery.
- D. There are too many small, inefficient, and under-utilized perinatal services.
- E. Perinatal education at all levels is inadequate.
- F. Financial support for perinatal services for medically indigent mothers is insufficient.

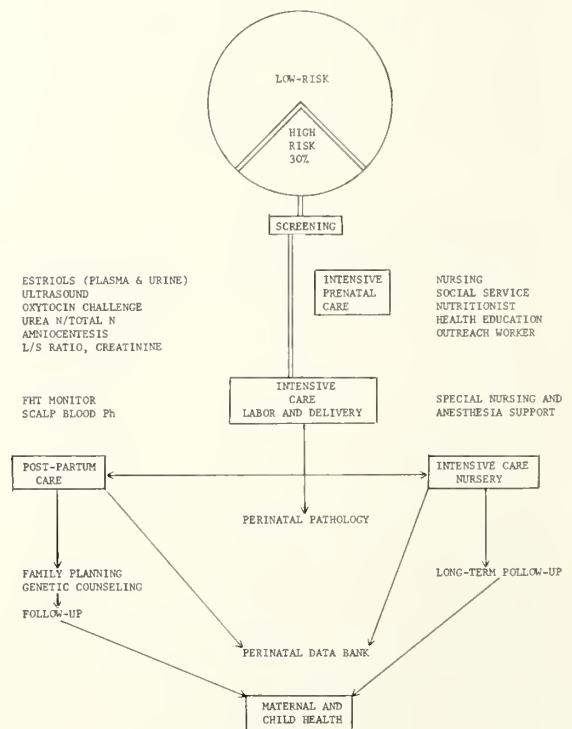


Figure V

PERINATAL MORTALITY IN CHARLESTON, SOUTH CAROLINA

A FOURTH CONSECUTIVE FIVE YEAR STUDY

1969-1973

HENRY C. HEINS, Jr., M.D., M.P.H.*

This is the fourth consecutive five-year study of perinatal mortality in Charleston County.^{1,2,3} This period of study extends from January 1, 1969, through December 31, 1973. The same definition is used for Perinatal Mortality I. This is defined as an infant weighing 1000 grams (2 lbs. 4 oz.) either stillborn or born alive that dies within the first seven days of life. This older definition is used for comparative purposes only. Most investigators of the problem today have changed to what is called Perinatal Mortality II. Perinatal Mortality II is defined as the loss of a product of conception weighing at least 500 grams (1 lb. 2 oz.) that is either born dead or dies within the first twenty-eight days of life. This latter definition is used by most states today, as well as most countries. Obviously, this is a much more comprehensive period of time in the perinatal period, and hence, the rates will be higher, both fetal and neonatal.

It doesn't take much imagination to realize that the mortality rate for infants weighing from 500 grams to 1000 grams will be extremely high (approximately 90%). Gestation agewise this period would cover from 20 weeks of pregnancy to 28 weeks of pregnancy.⁴

There occurred a total of 25,122 births weighing over 500 grams in this hospital study of which 246 weighed less than 1,000 grams.

Of the total 796 perinatal deaths, 236 weighed between 500 and 1,000 grams. It is estimated that these infants, weighing

500 to 1,000 grams made up less than one per cent of the total deliveries but accounted for more than 30 per cent of the perinatal deaths.

The births and deaths were again divided into white (15,389 with 294 deaths greater than 1,000 grams) and black (9,733 with 266 deaths greater than 1,000 grams).

The numbers of births, approximately 25,000, remain remarkably stabilized during each of the four five-year periods. This fourth study is the first time that the number of black perinatal deaths over 1,000 grams was less than white. (Perinatal Mortality I, see figure I.)

However, when all deaths over 500 grams were examined (Perinatal Mortality II), the number of black deaths is greater, despite fewer births — 15,389 whites and 9,733 blacks (see figure II, Perinatal Mortality II).

Rather than five maternity services, as in the previous three studies, only three hospitals within Charleston have obstetrical services at present.

Roper Hospital (7,591 births) is a pri-

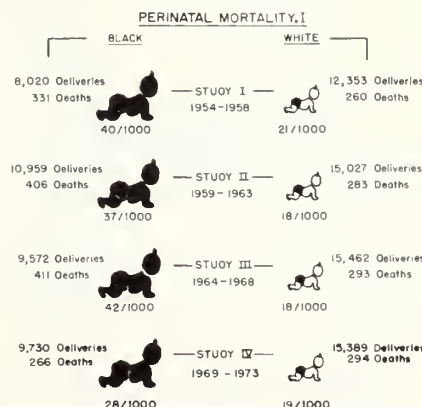


Figure I.

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Consultant, Maternal & Child Care Division, South Carolina Department of Health & Environmental Control

PERINATAL MORTALITY
FIGURE II. PERINATAL DEATHS BY RACE

TOTAL BIRTHS	WHITE	BLACK
greater than 500 gms.	15,389	9,733
500 gms. - 1000 gms.	110	136
1000 gms. - 2500 gms.	962	1,648
2500 gms. +	14,317	7,969
LBW %	7.4%	22%
FETAL DEATHS		
greater than 500 gms.	182 (11.8/1000)	212 (21.7/1000)
greater than 1000 gms.	142 (9.2/1000)	154 (16/1000)
NEONATAL DEATHS		
greater than 500 gms.	212 (13.9/1000)	190 (19.9/1000)
greater than 1000 gms.	152 (10/1000)	112 (11.8/1000)
Perinatal Mortality II	394 (25.6/1000)	402 (41.3/1000)
Perinatal Mortality I	294 (19.2/1000)	266 (27.7/1000)

vate hospital with 249 black deliveries. St. Francis Hospital, also a private hospital, (5,500 births) had 701 black births. Medical University of South Carolina is the chief location of black births (8,783) with some 3,248 white births

The significant difference is still by race and social status, not between hospital services. (See figure III.)

It is worthwhile to note the improvement in black rates during the last five years. This improvement is chiefly caused by fewer fetal deaths. The overall perinatal mortality (Perinatal Mortality I) for whites remains approximately the

same, that is 19 per 1,000 births, but the black improved some 30 per cent to 27.7 per 1,000. The fetal death ratio in the blacks improved some 40 per cent down to 16 per 1,000. (See figure IV.)

The deaths were analyzed by clinical cause as in the past studies using the classification of Nesbitt and Potter.^{5,6} Figures V and VI represent the categories of etiology, using numbers of deaths per 1,000 births in each category.

Potter believes that rather than give simply the number of deaths in a classification, or its percentage, a more accurate method of tabulation is the incidence per

FIGURE III. PERINATAL DEATHS OVER 500 GRAMS BY HOSPITAL

	ROPER	ST FRANCIS	MUSC
Deliveries Greater than 500 Grams	7,591	5,500	12,031
Perinatal Deaths	122	101	573
Perinatal Mortalities II	16/1000	18/1000	47/1000
Fetal Deaths	80	62	252
FMR	10.5/1000	11/1000	21/1000
Neonatal	42	39	321
NMR	5.5/1000	7/1000	26/1000
Autopsies	34	39	126
(TOTAL PERCENTAGES)	(28%)	(38%)	(22%)
Overall % = 25%			

PERINATAL MORTALITY

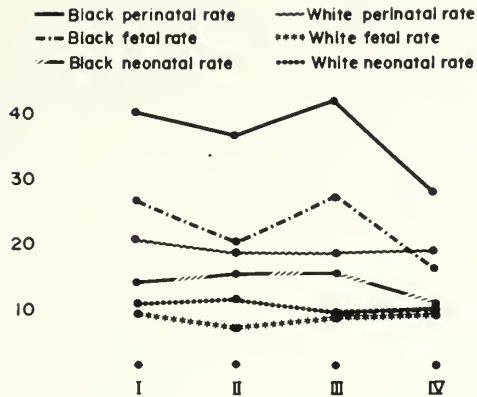


Figure IV.

thousand births.

Anoxia still is the leading cause of death in both white (4.8/1,000) and black (5.6/1,000). Abruptio of the placenta is the leading contributor to this group causing 42 white and 28 black deaths. In the previous 5 years there occurred 36 white and 81 black perinatal losses from this etiology. The smaller number in this study may reflect improvement in perinatal care with less so called toxemia of pregnancy (improved nutrition and/or better supervision in labor). Early diagnosis and timely intervention to effect delivery by the most conservative procedure may spare the fetus an anoxic death. In the occasional patient, the most conservative procedure may be abdominal delivery.

Placenta previa caused the deaths of only eight infants in our study (5 blacks, and 3 whites). This was an improvement from the 17 lost in the previous five years. Seven of the eight infants weighed less than 2,500 grams. A policy of expectant management after the diagnosis is confirmed by ultrasonic examination can be rewarded by avoidance of delivery of a low birth weight infant.⁷

Cord complications caused the deaths of 19 white and 13 black infants. This total group of 32 remains close to the total cord fatalities in the last study of 36 (12 white and 24 black). This accident should be detected earlier by closer monitoring of the patient and immediate delivery by Cesarean section, if the patient is not

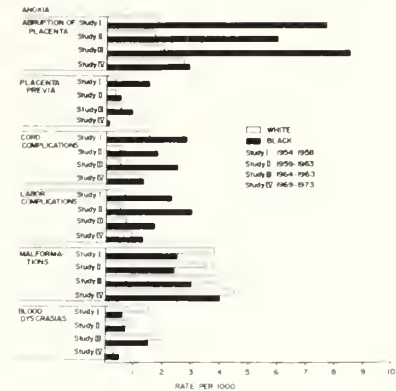


Figure V.

near full dilation.

Prolonged labor or complications of labor caused the deaths of 14 white and 13 black infants. In the previous study this diagnosis was made in 12 white and 17 black losses. Closer evaluation of the pelvis, use of fetal monitoring, both electronically and biochemically, should further reduce this number. The Cesarean section rate now approximates 10 per cent, where it was 5-6 per cent in the last study.

Major malformations continue to be a source of problems, still in larger numbers in the white (69 deaths) than the black (39 deaths). In the 1964-1968 study there were 62 white and 29 black deaths due to this cause. A careful medical, genetic and family history will often alert the obstetrician to this risk. The clinician

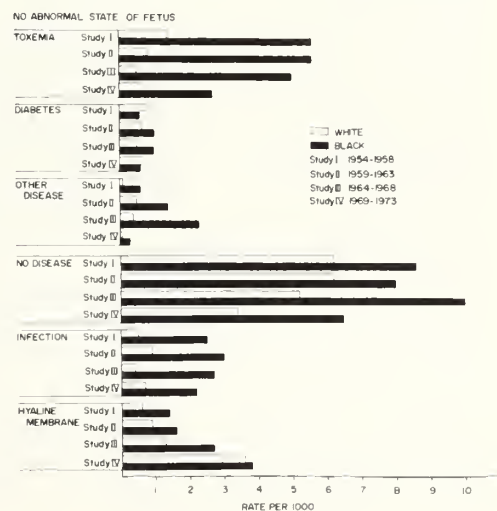


Figure VI

PERINATAL MORTALITY

should avoid radiation of his patient and be especially careful in administration of drugs in the first trimester.

Much improvement has been noted in the blood dyscrasia group. Six white and five black deaths were attributed to Rh incompatibility. In the previous period of study there were 33 white and 15 black deaths due to this cause. The chief reason for this reduction is the administration of Rhogam to the mother in the first 72 hours post-partum, to suppress specific immunological response to fetal Rh positive cells. The hospitals in Charleston give Rhogam to any unsensitized Rh negative mother who delivers a Rh positive infant (unless she signs a refusal to accept the treatment).

Sensitized Rh negative mothers are followed with antibody titres and amniocentesis. To minimize the risk of kernicterus particularly in an immature infant, the blood must be exchanged-transfused soon after birth and repeated as necessary. The indication for intrauterine transfusion of the fetus had dramatically lessened in the last five years.

In the large group of infants with no abnormal state, there were 11 white and 26 black deaths associated with toxemia of pregnancy. This was a decrease from the previous study of 8 white and 48 black deaths.

There is still a much higher incidence of toxemia in the black group of patients. Today, with the use of such parameters as plasma estriols, L/S ratios, oxytocin challenge test and ultrasound, a better determination of the fetal age and welfare can be done. This is very important at the timing of intervention.

There were 12 white and 6 black deaths described to diabetes mellitus in this study. This compares to 8 white and 12 black losses in the previous 5 year study. The trend continues to induce labor at 37-38 weeks gestation. If induction fails or the cervix is unfavorable, abdominal delivery is carried out.

The "with other disease" group was again made up chiefly of infants whose

mothers had renal disease. Pyelonephritis was again the most common diagnosis. Only 1 white and 3 black infants were in this group, compared to 7 white and 22 black losses previously.

The largest group of these infants without abnormal state was the group where the mother also had no disease. These are the patients who experienced early onset of labor with loss of a low birth weight infant. There were 53 white and 63 black infant deaths compared to 81 white and 104 black previously. The losses are divided equally between neonatals and fetals, but 75 per cent of them were between 1,000 and 2,500 grams.

The cause of premature labor is obscure, as is the cause of term labor. Again in this study, review of the charts reveal efforts to stop early labor with the use of opiates. In these cases the difficulty was compounded by delivery of a narcotized low birth weight infant.

In subsequent pregnancies, an attempt is being made to screen this type of mother into the high risk clinic where she is encouraged to increase bed rest with close check on her cervix for evidence of incompetence and possible surgical closure. She is also counselled in high protein diet and non-smoking in an attempt to add to birth weight.⁸

Infection was determined to be the cause of death in 11 white and 22 black compared to 6 white and 26 black deaths in the previous five years.

Intrauterine infection of the fetus most commonly takes the form of pneumonia and is usually caused by bacteria in the amniotic fluid which is aspirated by the fetus. Prolonged or desultory type labor may produce hypoxia in the fetus and increase this likelihood of aspiration.

After premature rupture of the membranes, antibiotic therapy throughout the latent period does not prevent intra-partum infection nor does it have a beneficial effect on reducing perinatal mortality. Antibiotics are usually administered intensively with the onset of labor into the puerperium. Infective lesions which

PERINATAL MORTALITY

cause death within the first 3-4 days after birth are usually ones contracted intra-partum. An infection relatively mild in a mature infant can be fatal to a low birth weight infant.

As might be expected, abnormal ventilation of the lungs such as hyaline membrane disease caused the deaths of 56 whites and 37 black infants compared to 20 white and 25 black infants in the previous five years. What probably accounts for the increased number is the wider classification of lung disease than strictly hyaline membrane disease. The vast majority of these infants were less than 2,500 grams.

There is improved survival in the neonatal intensive care unit with prevention of hypoglycemia and bilirubin problems, assisted respirations, and proper warmth. It is estimated that the survival rate has doubled since establishment of this unit in 1967.⁹

Why the improvement in the black rates with little, if any, improvement in the white? Many variables have to be studied when considering the improvement.

This five-year period of study is the first full five years of the MIC project in Charleston County. It would be simplistic to say that the maternal and infant care project was the complete answer. The perinatal mortality rates remain high in the black, much higher than in the white, for this group of patients taken care of in the Maternal and Infant Care Project.

There was a much greater number of patients served by the Family Planning Clinics—14,730, whereas only 7,500 were offered services in the previous five-year period.

Some 2,867 tubal ligations were done during this five-year period in both the blacks and the whites. Also, to be considered was a new alternative given the pregnant patient during this five-year period, that of voluntary abortion. Some 936 were done in the white group and 565 blacks made this choice during the past five years. This represents 1,528 high

risk (at least, unwanted) pregnancies.

How much of this improvement was due to the changing concepts of perinatal medicine? Someone has estimated the half life of perinatal information as being 18 months. The concept is of early identification of the high risk patient, and treating the patient not by the statistical approach as previously, but by using parameters such as estriols and ultrasound to consider each high risk patient individually.¹⁰ These helpful aids plus the use of the L/S ratio were important factors in timing intervention in problem pregnancies.¹¹

The use of fetal heart monitoring, scalp vein sampling, oxytocin challenge test, and ultrasound techniques of intensive supervision of patients. Whether good results obtainable with these techniques are due to close supervision of patients is not clear. No practitioner can, with the present state of the art, be considered negligent for not performing these tests. These tests are not to be used as replacements for clinical obstetrical judgment. A thorough menstrual history, a careful family and past history, careful examination of the uterine size (especially in the first 20 weeks of pregnancy) will be most helpful in care of the maternity patient.

One has to consider also approximately 1,000 blacks who were able to afford private care and received this care at Roper and St. Francis Hospitals. The perinatal mortality for these black patients was as good or better than the perinatal mortality rates for the white private patients. (See figure VII.)

FIGURE VII. Perinatal Mortality Rates
For 1000 Black Private Patients at
Roper and St. Francis Hospitals

Fetal Deaths—6 (3 less than 1000 Gms.)

FDR = 6/1000

Neonatal Deaths—7 (all less than 1000 Gms.)

NDR = 7/1000

Perinatal Mortality I = 3/1000

Perinatal Mortality II = 13/1000

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FIGURE VIII. Perinatal Mortality 7,178 Births USNH 1969-1973

Fetal Deaths—65 (15 less than 1000 Gms.)

FDR = 9/1000

Neonatal Deaths—50 (13 less than 1000 Gms.)

NDR = 7/1000

Perinatal Mortality I = 12/1000

Perinatal Mortality II = 16/1000

The births and perinatal deaths at the local Naval Hospital were studied for the first time during this five-year period. These 7,178 births were not included in the overall number of Charleston County births as the US Naval Hospital had not been included in previous studies. These patients are mentioned only to look at the maternity care given a group of patients where the cost of maternity care should not have been a very significant factor, if at all. (See figure VIII.)

There occurred 5 maternal deaths in Charleston during this five-year period, four black and one white. (See figure IX.) The present maternal mortality rate of 2/10,000 births ranks favorably with the national average.

The continuing decline in autopsy percentage at each hospital should be mentioned. This trend to a lower percentage is probably influenced by including births and deaths from 500 to 1,000 grams in this study. Few people are interested in postmortum examination of such an immature fetus, where little information is found in addition to the immaturity.

SUMMARY

1. The perinatal deaths for a fourth consecutive five-year period have been analyzed.

2. For the first time, an improvement has been noted in the black perinatal rates, especially the black fetal death ratio.

3. Perinatal mortality continues much higher for the black than the white. Speculation is raised that if the hazards of poor housing, poor nutrition, poor education, and lack of motivation could be removed, that the black rates would approximate the white.

4. Causes of perinatal mortality need to be identified because they must also be the causes of congenital handicaps in infants who do not die.

Is simple survival or death of a fetus too crude a parameter of reproductive performance?

MATERNAL MORTALITY









<u>BLACK</u>		<u>WHITE</u>
	STUDY I 1954-1958 15 MOTHERS DIED	
13		2
	STUDY II 1959-1963 10 MOTHERS DIED	
7		3
	STUDY III 1964-1968 8 MOTHERS DIED	
4		4
	STUDY IV 1969-1973 5 MOTHERS DIED	
4		1

Figure IX

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HOSPITAL SURVEY OF ACUTE PESTICIDE POISONING IN SOUTH CAROLINA

1971 - 1973

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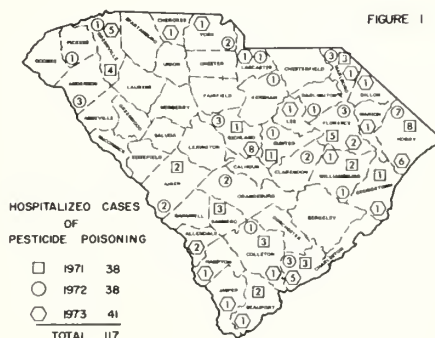
Acute poisonings by pesticides are a continuous problem in South Carolina and are of significant social concern to physicians, agricultural workers, pesticide formulators, commercial applicators, and the parents of small children. Pesticide morbidity in South Carolina has previously been explored by Keil, et al.¹ (1969) and Whitlock, et al.² (1971) utilizing a physician survey. Both studies found 600 patients per year treated by physicians for pesticide poisoning. To gain further insight about the extent of the problem, a three year retrospective study of hospitalized acute pesticide poisoning cases was conducted. The objectives of this study were: (1) determine the statewide incidence of hospitalized poisonings and (2) gain knowledge about the circumstances contributing to poisonings.

METHODS

All general hospitals in South Carolina were surveyed. Initially letters were sent to hospital administrators explaining the study objectives and requesting a medical records search for 1971, 1972 and 1973. Appropriate diagnostic codes were attached, and upon completion of the search each respondent returned a card listing the number of poisonings by year. From this information the geographic locations of the poisonings were identified and are depicted in Figure 1.

Each hospital reporting one or more poisonings for a year was personally visited by a field investigator to obtain information about length of stay, social

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factors, circumstances of the poisoning, type pesticide, symptoms, and treatment regimen. To avoid medical-legal conflicts, patients were not identified by name.

RESULTS AND DISCUSSION

Seventy-three of the State's seventy-six general hospitals cooperated in the survey for a 96 per cent response rate. Thirty-eight pesticide poisonings requiring hospitalization occurred in each of the years 1971 and 1972, but increased slightly (8%) to 41 in 1973. No deaths were recorded on the 117 cases reviewed and the length of stay for in-patient care averaged 3 days.

Patients hospitalized for pesticide poisoning are categorized into four types of exposure groups as found in Table 1. The majority of poisonings (37%) were of the occupational type, which included farmers, agricultural workers, commercial applicators, and pesticide formulators. Accidental poisoning of children accounted for 31 per cent of the total poisonings. In these cases the child accidentally found a container of pesticide around his home and was observed playing with or ingesting the chemical. Eighteen per cent

SURVEY OF ACUTE PESTICIDE POISONING

TABLE 1

TYPE OF EXPOSURE OF PATIENTS HOSPITALIZED FOR PESTICIDE POISONING IN SOUTH CAROLINA, 1971-1973

TYPE	1971		1972		1973		Combined	
	N	%	N	%	N	%	N	%
Occupational	11	30%	13	34%	19	46%	43	37%
Intentional (Suicidal)	8	21%	7	16%	6	15%	21	16%
CHILD (Accidental)	10	26%	13	34%	13	32%	36	31%
Non-Occupational (Adult)	6	16%	4	11%	3	7%	13	11%
Records not Available	3	7%	1	3%	0		4	3%
Total	38	100%	38	100%	41	100%	117	100%

of the poisonings were due to suicide attempts by adults. Fortunately these patients were found by relatives or friends after ingestion of the pesticide and were taken to the hospital. Non-occupational exposure in adults, such as spraying insecticides around the home, accounted for 11 per cent of all poisonings. Table 2 lists the poisonings by place of occurrence.

TABLE 2

PLACE OF POISONING OF PATIENTS HOSPITALIZED FOR PESTICIDE POISONING IN SOUTH CAROLINA, 1971-1973

PLACE	1971	1972	1973	Combined	
	%	%	%	N	%
Home	42%	50%	46%	54	46%
Work	34%	37%	41%	44	38%
Unknown	24%	13%	10%	18	15%
Other			3%	1	1%
Total	100%	100%	100%	117	100%

The age distribution of patients hospitalized for pesticide poisoning (Figure 2) ranges from 1 to 81 years of age with the mean age of 22.2. Children between ages of 0-5 accounted for the greatest percentage of pesticide poisoning. The age increments of 6-10 and 11-15 contain accidental poisoning to children, but also

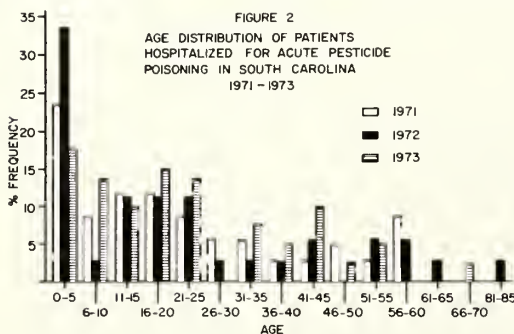
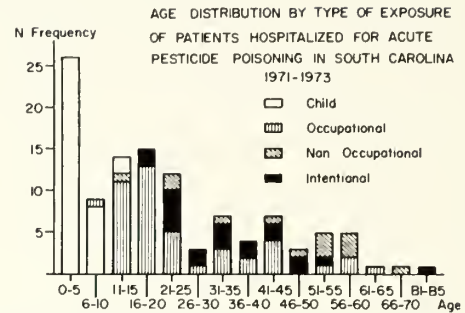


FIGURE 3



include children who were "cropping" tobacco (occupational) at the time of their exposure. The 16 and above age groups represent the occupational, non-occupational, and suicidal exposure. The largest number of suicide attempts (five patients) were in the 21-25 age group.

Table 3 presents a sex and race distribution of poisoning and shows an almost constant ratio (7:3) of male to female cases over the survey period. The number of poisonings in the black population increased sharply from 1971 to 1973 because a family with six children was poisoned by Parathion.

Poisoning routes, whether oral, dermal, respiratory, or combinations of these, are shown in Table 4. Incomplete medical records often made it difficult to retrieve the route of exposure and, in many of the occupational poisonings, the patient had no knowledge of how he was poisoned. To reduce bias, the route of exposure was noted only when clearly stated in the patient's record.

Table 5 lists the ten most reported symptoms of pesticide poisoned patients upon admission to the hospital. Twenty-six patients (23%) were asymptomatic, 25 of these having ingested the pesticide (15

TABLE 3

SEX AND RACE DISTRIBUTION OF PATIENTS HOSPITALIZED FOR PESTICIDE POISONING IN SOUTH CAROLINA, 1971-1973

YEAR	PATIENTS	MALE			FEMALE			TOTAL	
		WHITE N	BLACK N	% MALE	WHITE N	BLACK N	% FEMALE	% WHITE	% BLACK
1971	38	17	7	71%	7	3	29%	71%	29%
1972	38	19	8	73%	7	3	27%	70%	30%
1973	41	20	10	73%	6	5	27%	63%	37%

* 4 Patient Data Unavailable for 1971 and 1 patient data for 1972.

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TABLE 4

ROUTES OF EXPOSURE OF PATIENTS HOSPITALIZED FOR PESTICIDE
POISONING IN SOUTH CAROLINA, 1971-1973

ROUTES	1971	1972	1973
Oral	16	19	13
Dermal	2	2	3
Respiratory	4	4	3
Oral - Dermal	1	1	1
Dermal - Respiratory	3	2	3
Oral - Dermal - Respiratory	0	0	1
Unknown	9	9	17
Records Unavailable	3	1	0
Total	38	38	41

children plus 10 suicide attempts). One industrial worker was treated at the site of the exposure before admission to the hospital. Greater awareness of the hazards of pesticides by the public and medical community as well as availability of antidotes and prompt action by physicians probably account for poisonings not progressing to the sign and symptom stage. Children who ingested the pesticides were taken almost immediately by their parents to the hospital for emergency treatment. The ten who attempted suicide usually boasted to family or friends shortly after ingesting the pesticide and were rushed to the hospital.

A listing of the pesticides which poisoned the 117 patients hospitalized from 1971 through 1973 is found in Table 6. Hospitalized cases due to organophosphates increased by 26 per cent in 1973 when compared to 1971. Parathion, an organophosphate pesticide, accounted for 27 per cent of all poisonings. Chemicals listed as "tobacco" and "cotton poison" are thought to be of the organophosphate type, and when included with that group suggest that 54 per cent of all the poisonings may be attributed to organophos-

TABLE 6

Causative Agents of Patients Hospitalized for Pesticide
Poisoning in South Carolina, 1971-1973

CHEMICAL	1971	1972	1973
Insecticides			
Organophosphates			
Parathion(ethyl & methyl)	9	9	14
Malathion	0	1	1
Diazinon	2	2	2
Hot Shot Bug Killer (Diazinon)	0	1	0
Azodrin	0	1	0
Di-syston	0	1	0
Drtho-isotox	0	1	0
Guthion	0	0	1
"Tobacco Poison"	7	4	3
"Cotton Poison"	1	0	0
Other organophosphates	0	0	3
Chlorinated Hydrocarbons			
Toxaphene	1	1	0
Chlordane	2	0	1
Aldrin	1	0	0
Pentachlorophenol	0	0	1
Mirex	0	0	1
Carbamates			
Lannate	1	0	4
Sevin	1	0	0
Other			
Hot Shot House & Garden	1	0	0
Real Kill House & Garden	0	1	0
Raid	0	0	1
Paris Green	0	1	0
Sodium Fluoroacetate	0	0	1
Black Flag	1	2	1
Roach Kill	2	0	0
Cyanogas	0	1	0
"Soy Bean Dust"	0	1	0
Flux Dip (CH-OP)	0	1	0
Termite Spray	0	0	1
Roach Tablets	1	1	0
Rodenticides			
"Rat Poison"	1	4	0
D-Con	0	2	1
Warfarin	0	1	2
Prolin Rat Bait	0	0	1
Arsenic	1	0	0
Strychnine	1	0	0
Herbicides			
Unknown	0	0	1
Records Unavailable	2	0	0
	3	1	0
Total	38	38	41

phates. The chemicals listed represent a diffuse list of toxins which were intended for insecticide, rodenticide, and herbicide purposes and were found in liquid, dust, spray and granular forms.

Following are four case reports which are typical of the types of exposure as found in Table 1:

1. Occupational

A 22-year-old white male helicopter pilot was spraying crops with Parathion, Toxaphene and DDT on the day of admission to the hospital. While flying his helicopter the patient became ill from inhalation of the spray and recognized his symptoms to be those of organophosphate poisoning. He immediately took 2 atropine pills (antidote for organophosphate poisoning) and was taken to a hospital. His symptoms upon arrival were dizziness, nausea, vomiting, weakness and grogginess. He was released from the hospital fully recovered in one day.

2. Intentional (Suicidal)

A 25-year-old black female ingested an unknown quantity of Diazinon because

TABLE 5

TEN MOST COMMON SYMPTOMS OF PATIENTS HOSPITALIZED FOR
PESTICIDE POISONING IN SOUTH CAROLINA, 1971-1973

SYMPTOM	1971	1972	1973	Total
1. Vomiting	14	13	17	44
2. Abdominal pain, cramp	10	6	10	26
3. Nausea	6	9	10	25
4. Weakness	6	3	10	19
5. Constricted pupils	4	6	9	19
6. Tremor, fasciculations	3	6	3	12
7. Headache	5	4	3	12
8. Increased salivation	4	1	5	10
9. Difficult breathing & shortness of breath	4	4	2	10
10. Diarrhea	4	1	5	10

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of distress over the recent death of her brother. She was taken to a hospital shortly after ingesting the chemical and upon arrival gastric lavage and atropine were administered. The patient's only complaint was diarrhea, which progressed into acute renal insufficiency and shut down. This required the patient to be hospitalized for a period of ten days, after which she was released in good health.

3. *Child (accidental)*

A 5-year-old white male ingested a mouthful of roach poison containing Diazinon. The poison was left in a bottle on the kitchen stove by the child's mother and when she returned, approximately 10 minutes later, she found the child with the bottle. The mother gave her child milk to induce vomiting, but 10 minutes later the child went limp and was taken to a hospital. On admission to the hospital the child had complaints of increased sweating and salivation, vomiting, abdominal pain, tremors, drowsiness, slowing pulse and myotic pupils. Emergency measures were instituted and the child was released fully recovered in four days.

4. *Non-occupational (adult)*

A 43-year-old white male recently had his house treated for termites. The fumes from the termite spray were irritating his family so he crawled underneath his house to investigate. He reportedly became over-powered by the fumes and had to be dragged from underneath the house in a semiconscious condition by a member of his family. He was rushed to a hospital and was semiconscious with myotic pupils upon arrival. Medical treatment was administered and he was released in two days fully recovered.

SUMMARY AND CONCLUSIONS

Seventy-three general hospitals in South Carolina reported 117 in-patient cases of pesticide poisoning from 1971 through

1973. Occupational poisonings have increased steadily and account for over one-third of the poisonings, while non-occupational poisonings have decreased and represent 11 per cent of the cases. Poisoning occurring in children constituted almost one-third of the total and 18 per cent proved to be suicide attempts.

If one accepts the findings of the studies of Keil and Whitlock, at least a 15 to 1 ratio is observed between patients treated by physicians and patients admitted to a hospital. Increased awareness among physicians and emergency room personnel may allow for many cases having been treated on an out-patient basis, while only the more serious cases were admitted to a hospital.

There has been an increase in the number of occupational poisonings from 1971 when only 30 per cent of all poisonings were occupational to 1973 when 46 per cent of pesticide poisonings were occupational in nature. Conceivably this could be accounted for by the use of alternate chemicals when DDT was banned by EPA in 1972.³ Often substitutes for DDT are highly toxic organophosphates which the occupational users (formulators and farmers) must employ. Thus as more organophosphates are applied, the risk to the users increases.

ACKNOWLEDGMENTS

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LONG-TERM FOLLOW-UP OF SURVIVORS OF ACUTE PESTICIDE POISONING

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Increasing awareness and interest in the field of community and environmental health has focused the attention of many investigators on acute pesticide poisonings. Most poisoning reports to date have considered the etiology and initial treatment, with few mentioning the long-term follow-up of poisoning cases.

In an attempt to identify any lasting sequelae, eight persons (described in Table 1) known to have been treated for acute pesticide poisoning in South Carolina were interviewed and examined. Six of the patients seen had been poisoned with organic phosphate compounds, one by a chlorinated hydrocarbon and one by fluoroacetate; the longest interval be-

tween time of poisoning and time of current study was four years, the shortest interval eight months. One patient was a 23-year-old male, the rest, children under the age of eight years.

METHODS

All patients studied represented severe acute poisoning. Each had demonstrated symptoms of severity sufficient to require immediate medical attention and hospitalization. Most required intensive medical care and several were comatose for a significant period of time.

The evaluation process included an interview session, complete physical examination, and extensive laboratory testing. Medical, social, and family histories

TABLE I
DESCRIPTION OF PATIENTS

Patient	Age (Years)	Sex	Race	Interval Since Poisoning
#1	1-2/12	F	W	18 months
#2	2	F	B	9 months
#3	3	M	B	12 months
#4	3	M	B	27 months
#5	6-7/12	M	W	14 months
#6	6-10/12	M	B	48 months
#7	7	F	B	45 months
#8	23	M	W	13 months

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as well as self-evaluation of any poisoning sequelae were elicited from each patient or his parents. Historical areas specifically explored included the presence of persistent nausea, headaches, insomnia, muscle weakness or fatigue, blurred vision, psychiatric disorders, or intolerance to further pesticide exposure.

FOLLOW-UP OF ACUTE PESTICIDE POISONING

The physical and neurological examinations followed the outline provided by the Environmental Protection Agency Division of Pesticide Community Studies. Particular attention was devoted to examination for dermatitis, visual problems, pulmonary impairment, or abnormal motor function. When practical, the Denver Developmental Screening Test was administered. A standard (12 lead) electrocardiogram was also obtained on each participant.

Laboratory studies included a complete blood count and measurements of blood levels of pesticide residue, calcium, phosphorus, bilirubin, urea nitrogen, creatinine, glucose, total protein, serum albumin, uric acid, lactic dehydrogenase, SGPT and SGOT; and urinalysis for glucosuria, albuminuria, acetonuria, and urine pH were also performed.

RESULTS

Patient histories, summarized in Table 2, revealed that one individual (patient #7) had been treated three separate times

over a four-year span for a syndrome resembling acute toxin ingestion. Dieldrin, a chlorinated hydrocarbon pesticide, was the only substance identified in the home and its ingestion was suggested by elevated blood levels of this compound on one of the three admissions. The initial admission was precipitated by the onset of anuria, vomiting, and extreme lethargy. Peritoneal dialysis led to marked improvement.

The same set of symptoms led to the second hospitalization six months later; improvement again was remarkable with dialysis. No dialysis was performed upon the third admission 29 months later at another hospital, apparently because anuria was not evident in an otherwise identical syndrome. In none of these acute episodes was there clear history of ingestion of toxin although the patient's mother indicated that the child could conceivably have had access to toxic substances on each occasion. An insecticide known to contain Dieldrin was identified

TABLE II
FINDINGS AT
FOLLOW-UP EXAMINATION

Patient	Pesticide	History	Physical Exam	Lab
#1	Fluoroacetate	Unremarkable	WNL	WNL
#2	Diazinon	Unremarkable	WNL	WNL
#3	Parathion	Temper tantrums; irritability	Difficulty with maternal separation; un-cooperation	WNL
#4	Parathion	Excitability; emotionally less stable than siblings	WNL	WNL
#5	Diazinon	Hyperactivity; Limited attention span	Fine motor difficulty; hyperactivity	WNL
#6	Diazinon	Unremarkable	WNL	WNL
#7	Dieldrin	Hospitalized X3 for symptoms attributed to acute toxin ingestion	WNL	WNL
#8	Azodrin	Unremarkable	WNL	WNL

FOLLOW-UP OF ACUTE PESTICIDE POISONING

in the blood by the method utilized by Dale *et al*¹ at a level of 11.6 PPB in one of five daily samples of blood. All others tested as "trace."

Despite the discharge diagnosis of acute toxin ingestion in this case, the evidence for such a poisoning appears ambiguous. The levels of Dieldrin reported are not consistent with the findings of Jager,² who has reported with considerable substantiation a threshold blood level of about 150-200 PPB for Dieldrin toxicity. It seems worthwhile to note that Jager also described a series of independent studies of blood pesticide levels of a total of over 200 apparently healthy members of the general population in the United States and Great Britain from 1962-1968. The mean Dieldrin level of each study fell generally around 2 PPB, with no reading as high as 12 PPB.

Anuria, described in two of patient #7's admissions, is not usually associated with acute Dieldrin poisoning, although the remaining symptoms of lethargy, vomiting, and malaise are often reported. In a study of 100 persons occupationally exposed to pesticides, Davies *et al*³ noted a relationship between chronic pesticide exposure and renal tubular malfunction. They found problems with urine concentration and tubular phosphorus reabsorption, but no specific indications of oliguria or anuria.

The current physical examination and urinalysis evidence no extraordinary findings for this patient. Kidney and neuromuscular function appeared to be within normal limits. We have concluded in this patient that her symptomatology was most probably not secondary to Dieldrin intoxication, but have included her in the study because she carries this diagnosis in her medical history.

No subsequent incidents of medical significance were evident in other histories, although a small number of chronic complaints were noted.

The parents of three of the children tested (#3, #4, #5) indicated an increased

degree of excitability and nervousness among the poisoned children distinct from the behavior of their siblings. Only one child (patient #3) was actually characterized as having become more nervous and emotionally less stable since the instance of poisoning. The mother of the child in question seemed convinced that the toxicant ingestion was at least partially causative. With the exception previously noted, none of the patients had had any exposure to pesticides since their hospitalization.

From one to three days immediately following hospital discharge, minor symptoms including ataxia and general muscular weakness were noted by three patients.

Physical and neurological examinations were within normal limits for most areas, including the specific ones mentioned above. Patient #5, described by his mother as being abnormally nervous and hyperactive, was intensively examined to detect fine and gross motor irregularities. Major motor function seemed normal, but the patient had difficulty with fine coordination, rapid alternating movements, and simultaneous use of both hands. These problems, however, antedated ingestion of Diazinon according to the patient's parents. The diagnostic impression was minimal brain dysfunction with hyperactivity.

EKG data evidenced no abnormalities in any patient. A physiologic S-T segment elevation was seen in patient #8 with no history of apparent cardiorespiratory problems other than a brief episode of asthma. Results of blood and urine analyses fell essentially within normal limits.

DISCUSSION

Discounting the suspected case of minimal brain dysfunction, two individuals, patients #3 and #4, manifested neurological and/or psychiatric patterns which were interpreted as abnormal by their respective parents. Coincidentally, both were Negro males three years of age poisoned with Parathion, an organic

FOLLOW-UP OF ACUTE PESTICIDE POISONING

phosphate pesticide. During the examination period, #3 exhibited highly pronounced unwillingness to separate from his mother and was completely uncooperative in the administration of the Denver Developmental Test. His mother believed this type of behavior to be a direct result of the poisoning.

The behavior of #4 was not abnormal in any respect during the examination process, although his father described him as being noticeably irritable and overly sensitive to frustration of motives.

It is interesting to note that in a number of other studies related to phosphate ester pesticides, similar persistent characteristics were noted in persons who had been treated for acute poisoning. Tabershaw and Cooper⁴ found complaints of nervousness and irritability persisting for more than three years in six of 114 individuals examined following an acute episode of pesticide poisoning. However, none of the six attributed the symptoms directly to the poisoning incident. More than half of the 114 cases did not require hospitalization and subsequently would not have qualified for a description of acute poisoning according to the criteria utilized in this study.

An investigation by Metcalf and Holmes⁵ of seventy men with histories of exposure to organophosphate pesticides revealed eleven subjects who reported problems with increased irritability and nervousness. Nine of the eleven had suffered severe or multiple exposures.

A marked increase in irritability was among the symptoms induced in otherwise normal-appearing subjects exposed to an organic phosphate in a study performed by Rowntree, Nevin, and Wilson.⁶ The individuals were given a total of 13 mg. of isopropylfluorophosphonate over a period of seven days. The induced abnormalities apparently disappeared, however, shortly after withdrawal of the

drug.

In many investigations of long-term sequelae of pesticide poisonings, a high incidence of mental confusion has been a frequent disturbance noted. Durham found that lapses of attention led to the majority of the confusion often displayed by agricultural workers who had been poisoned by pesticides. The studies by Tabershaw and Metcalf mentioned above indicated similar findings, although Rowntree noted a marked absence of any mental disorientation in the subjects given DFP. The ages of the patients involved in the present study precluded any serious consideration of testing for similar characteristics.

While there is a suggestion of some behavior changes in one or two of our patients, it is difficult to assess changes in behavior relative to a baseline which is necessarily historical. "Soft" neurological data of this type, obviously, does not readily lend itself to analysis and evaluation. Our laboratory, physical, and behavioral examinations have identified no definite chronic disorders following acute pesticide ingestion or exposure in these patients. No correlation of pesticide exposure with abnormal heme synthesis was noted, confirming Embry's⁸ studies.

SUMMARY

Physical examination as well as laboratory and behavioral studies have identified no chronic disorders in eight persons following acute pesticide exposure despite an illness⁷ sufficient to require intensive medical care. Six of the patients had organophosphate exposure, one Dieldrin, and one fluoroacetate. While certain manifestations of behavioral patterns may be consistent with findings of other investigators, the evidence is inconclusive regarding long-term sequelae in these patients. It appears that early aggressive medical care can result in a complete recovery in many such patients.

FOLLOW-UP OF ACUTE PESTICIDE POISONING

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ACCREDITED BY THE J. C. A. H.

President's Pages



Dear Fellow Physicians:

The activities of the South Carolina Medical Association are moving along at a rapid pace since my report to you in the last issue of *The Journal*. We have had a joint meeting with the Insurance Commissioner and with several neurosurgeons involved in trying to equalize the liability payments. As a result of this meeting it was found that the anesthesiologists and the neurosurgeons had had a 50% surcharge added to their premiums. This was removed, reducing the premiums of these two specialists. All of the other premiums remain the same. This schedule has been officially published and is available for everyone's perusal.

On July 28, Dr. Kilgore and Charlie Johnson attended a liability seminar put on by the AMA and the American Hospital Association in Chicago to discuss the liability problem. Your president attended a seminar sponsored by the S. C. Insurance Commission at Hilton Head on Tuesday, August 12, and it was an enlightening experience to hear the various disciplines speak about the problems from their standpoint involving the Medical Association, the Insurance Industry, the Trial Lawyers' Association, the Insurance Commissioners, and the U. S. Congressional scene. More will be forthcoming on this problem.

Dr. Kilgore's Professional Liability Committee has been very active and has had one meeting and has another meeting scheduled for August 21. There are plans to have a joint meeting of the Professional Liability Committee, the Public Relations Committee, on September 11 at the headquarters in Columbia to outline our program of action for the entire Medical Association, and to get the message across to the public and to the legislators in the coming months. We ask each and every one of you serving on these committees to make plans now to attend these meetings, to contribute your ideas, and to go back home afterwards and spread the message.

Council has had a session on August 13, and of prime importance at that meeting was the discussion on the permanent home of our new Medical Association building in Columbia. Due to the rising costs of inflation with the electricity and other costs involved, and due to the recession with the inability to rent the space in the building as had been planned, the building is in a deficit situation and will have to be financed on a long-term basis beyond that of the permanent loan. At its session on August 13, Council voted unanimously to ask for the House of Delegates to extend the special assessment of \$60 per year for three more years. This would give the Association a period of four years of stability in paying the costs of operation of the building, and, at that time, we would be able to carry forward on the previous financing arrangements. There may pos-

sibly be a special call for a House of Delegates meeting in September of 1975 to discuss this important item. Please discuss this with your representatives on Council and with any other officers or members who are knowledgeable in the situation and plan to attend this special meeting if and when it is called. This is a most urgent matter and will need the careful consideration of all involved.

On August 15, 16, and 17, a training conference is being held in Charleston. Twenty-three of our members will be taking the special course being put on by representatives of the AMA to teach our members proper techniques in interviewing the media and appearing on radio and TV seminar type programs. We know that much benefit will be gained from this session.

We are happy to report that the membership of the Association is ahead of the membership at this time last year and the affairs of the Association are progressing well. The officers and members of Council are working hard to do the job necessary to maintain the activities of our Association and we ask each and every member of the Association to participate in his committee assignment and to help in every way possible to forward the aims of the Association and the medical profession in South Carolina. Only through a united effort can we get the job done and continue to maintain our ability to give quality medical care on a private practice basis to the citizens of South Carolina.

Sincerely yours,
C. Tucker Weston, M.D.
President



50 YEARS AGO

August 1925

The decision of the Shriners to erect a hospital for crippled children was announced. A new tuberculosis hospital was under construction at State Park.

Rocky Mountain Spotted Fever Advisory

This is the time of year to increase the index of suspicion for Rocky Mountain Spotted Fever, also called tick typhus or American tick-borne spotted fever.

The South Carolina Department of Health and Environmental Control (DHEC) has observed a significant increase in the incidence of Rocky Mountain Spotted Fever in the state during the past 6 years. The first cases are usually reported in early May, with the peak number of cases coming in August.

Physicians are asked to be on the alert for febrile illnesses which follow tick bites or exposure in tick-infested areas. When Rocky Mountain Spotted Fever is suspected, serological confirmation is available from the Department of Health and Environmental Control Laboratory at 2600 Bull Street in Columbia. At least 2 serum specimens, collected 2 weeks apart, should be submitted to the State Laboratory in order to determine a rise in antibody titer. All cases should be reported to the DHEC Division of Epidemiology via the local county health department.

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Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

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*

WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

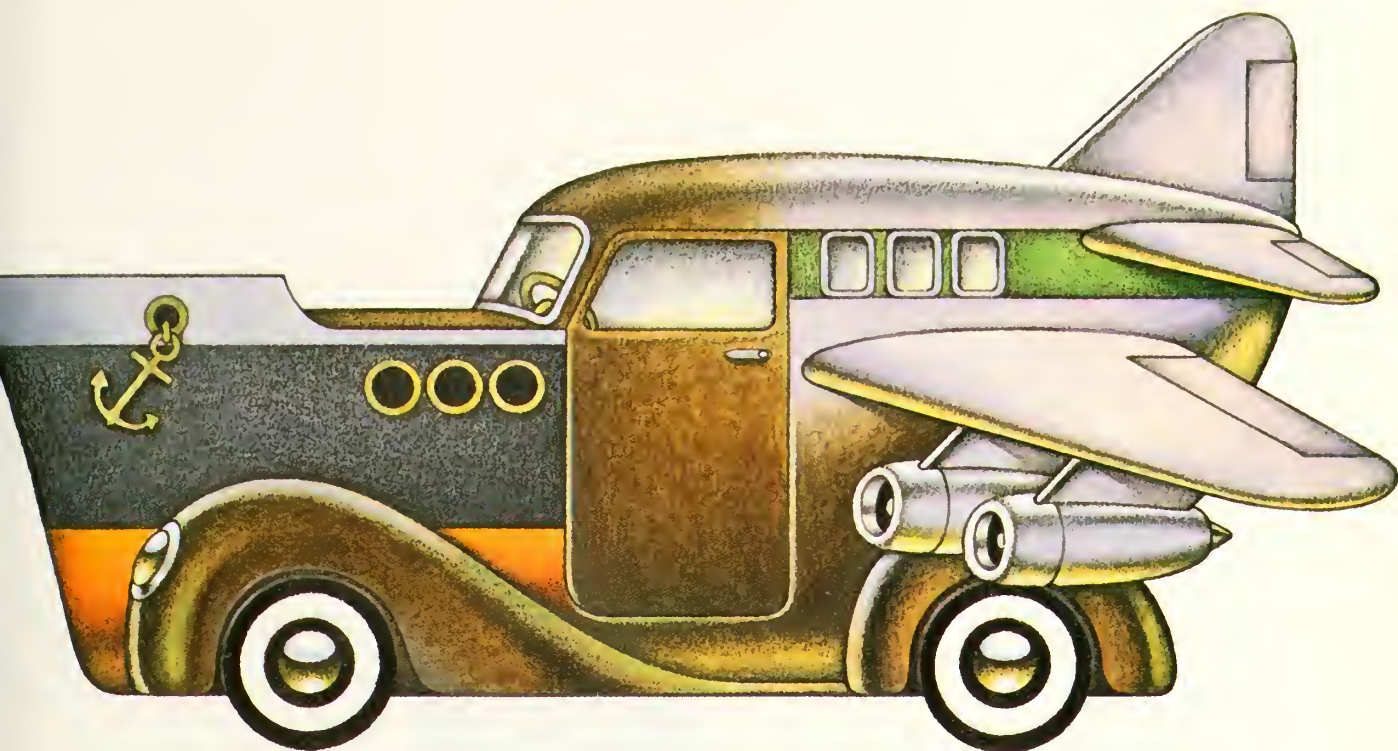
Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

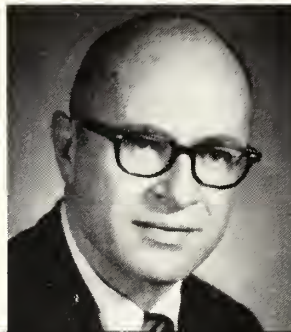
ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

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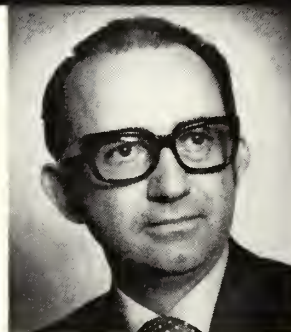
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Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

in purpose of drug information the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with an agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it should depend on the medication in question. For example, in the case of an injectable long-acting progestone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a longer one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and be removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

by the doctor can remove that fear of 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient about the incidence of serious adverse reactions, then you have to tell him about a concerned medical decision made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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Editorials

A Doctor is a Doctor is a Doctor

"The interests of the patient-consumer must be paramount over those of the health care provider, lawyer, or insurance carrier."

Whose words are these? Although rather Naderish in style ("patient-consumer" for patient, "health care provider" for doctor), this quote sounds like something you would expect from the AMA, the SCMA, or some other physicians group. Instead, it is the position of the American Trial Lawyer's (litigation advice vendors) Association in the malpractice brouhaha. I would say that this sounds like a very responsible position except that the lawyers' ideas of what are the patients' interests strangely coincide with the lawyers' interests—only I want to be responsible in my statement and do not want to pit doctors and lawyers in an adversarial relationship. In fact, on the advice of a very esteemed colleague and because I believe *most* lawyers, like *most* doctors, have to make a living but when it comes down to a choice between profit and morality, would always choose to be honest. There are only a very few in each profession that choose to be otherwise. It is difficult for me to write about dishonest lawyers, just as it is difficult and obnoxious to contemplate dishonest physicians. But what was originally intended to be a mild and clever divertissement—the use of the term "litigation advice vendor" for lawyer has completely changed my train of thought. It is much less offensive to assail litigation advice vendors than it is to assault lawyers. Come to think of it, in any (malpractice) litigation, both the plaintiff and the defendant must hire a team of litigation advice vendors and the proceedings must be presided by a

litigation advice moderator (judge), all of whose livelihoods are enhanced by such actions. Little wonder that a legislature jam-packed with litigation advice benefactors would be reluctant to take steps to reduce litigation, just or unjust.

Well, we started out to reinforce what The Wall Street Journal said: "Our Society has granted broad self-regulatory rights along with professional status to both medicine and the law. Those rights are being steadily withdrawn by the state and with them institutional freedoms that have had importance to the larger society.

"It would be a hopeful sign if the two professions could come to terms with each other and with the need to better police their own ranks. No one will gain ultimately from the adversary approach."

We had intended to plead for a reconciliation between the two great professions of medicine and law. Instead we have done the contrary. But perhaps we have demonstrated one thing. It is much easier to denigrate a litigation advice vendor than it is to blaspheme a lawyer. By the same token, we should absolutely reject the characterization of our healing profession as "health care providers." WE ARE DOCTORS!!! And our patients are PATIENTS, not consumers, or even "patient-consumers." Who ever heard of a provider-consumer relationship of real value? Who ever had rapport with a health care provider? I wonder if it is not a maliciously conceived scheme to substitute the concept of "health care provider" for "doctor." I have proved to myself it is much easier to condemn this dyslogia. Let's insist on being doctors! A doctor is a doctor is a doctor!

EEK

Is OB Leading the Way?

The two articles about perinatal health in this issue of JSCMA, it seems to me, have significance reaching far beyond the practice of obstetrics. Perhaps because perinatal mortality is clearly defined, can be easily expressed in rates per 1000 (Heins' two papers would have been clearer if he had used the rate per 1000 consistently rather than use gross numbers at important junctures) and these rates compared between hospitals and between population groups, or perhaps because the obstetricians are thinking ahead of the rest of us (maybe they have trouble sleeping while waiting on the last few centimeters of dilatation & think then), at any rate, obstetrical reasoning has described the most compelling support for regionalization of health care in South Carolina.

Heins quite clearly demonstrates, I think, why it would be advantageous to have 3 regional hospitals sitting at the top of the pyramid, supported by 10 to 12 district hospitals and 20 to 25 community hospitals. It makes good economic sense and good medical sense. Heins anticipates some of the problems such as patient acceptance and doctor cooperation. I would hope the obvious advantages would ensure this.

A disturbing fact revealed but not explained in Heins' first article is the North Carolina's fetal death rate is 78% of South Carolina's.

Heins' second article has implications reaching far beyond obstetrics and even far beyond medical care. American medicine critics often gleefully point to our infant mortality being around fifteenth or twentieth in the world, and blame this on "poor health care delivery." Heins has

demonstrated convincingly that other factors have great influence in fetal mortality.

For the first time in four consecutive five-year studies, this study showed fewer black deaths than white deaths in the over 1000 gram fetus group. The improving socioeconomic status of blacks in Charleston is partly, if not entirely accountable for this.

Another consideration is that fetal death rate for the white population is near the national average while South Carolina as a whole ranks third from the bottom in the United States' perinatal mortality. Yet, the approximately 1000 blacks who were able to afford private care had as good or better perinatal mortality rates as the white private patients. Again, factors other than medical care must be involved in the high perinatal mortality in the poor black cases.

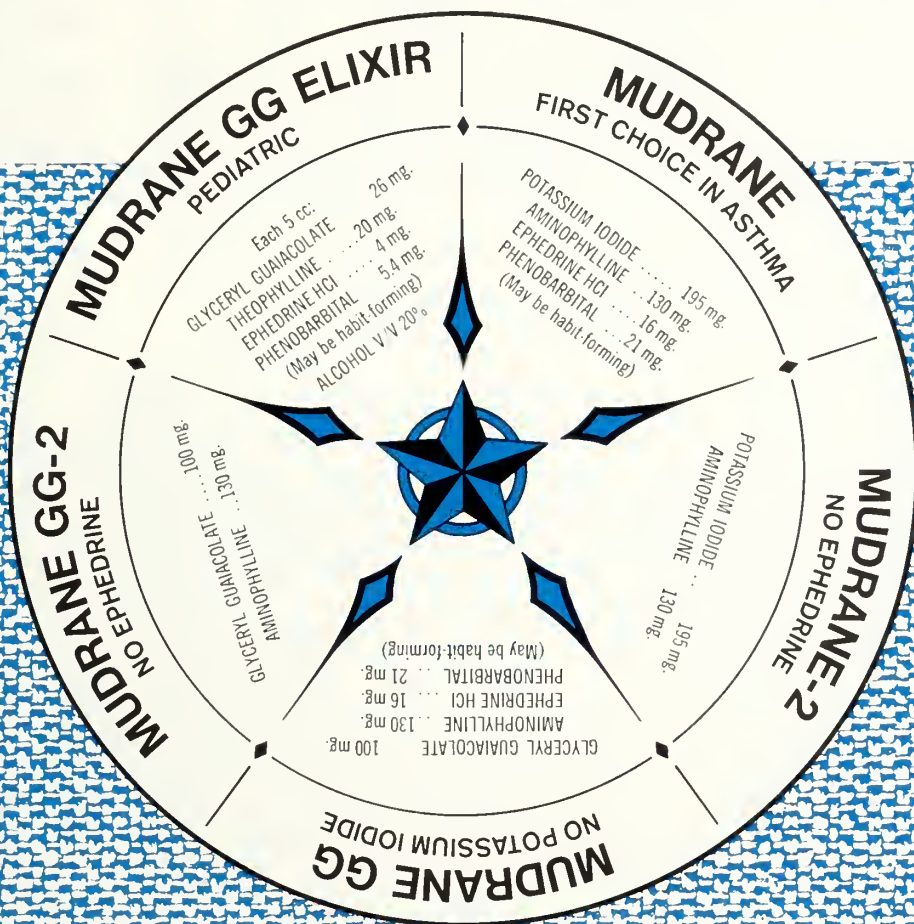
Again, perinatal mortality at the U.S. Naval Hospital, where cost and availability of medical care should have been no limit, was slightly worse than the black private patients and all private patients, but much better than in the class of patients that had to seek free care at MUSC.

These remarks are in no way intended to exonerate American physicians from some blame for our high perinatal mortality nor to excuse South Carolina physicians for our own abysmal record. It is meant to point out that other factors beyond our control are at play. But it is our responsibility to investigate, delineate, and strive to eliminate the factors outside medicine that contribute to perinatal mortality. Henry Heins has done much to further this by these reports.

EEK

The MUDRANES

Discreet formulations of four well regarded drugs for the relief of bronchial distress—Potassium Iodide, Glyceryl Guaiacolate, Aminophylline, Ephedrine with Phenobarbital (to lessen cardiac stimulation).



INDICATIONS: For the prompt symptomatic relief of bronchial asthma, emphysema and bronchiectasis. The Mudranes dilate the bronchi and liquefy mucus plugs. **DOSAGE:** Tablet; One tablet with a full glass of water 3 or 4 times daily as required. Divide tablet for child's dose. Elixir; Children, 1 cc for each 10 lbs. of body weight. May be repeated 3 or 4 times a day. Adult, one tablespoonful 4 times daily. All doses should be followed with a glass of water.

CONTRAINDICATIONS: Aminophylline/Theophylline is contraindicated in the presence of severe cardiac arrhythmias and patients with massive myocardial damage. Ephedrine, in presence of severe heart disease, extreme hypertension, and in hyperthyroidism. Phenobarbital, in porphyria and in patients with known phenobarbital sensitivity. Potassium Iodide, in pregnancy (to protect the fetus against possible iodine-induced depression of thyroid activity), in tuberculosis (produces gumma dissolution), and in acne; also in the presence of known iodide sensitivity. **PRECAUTIONS:** Aminophylline/Theophylline should be avoided in patients with massive myocardial damage and/or severe cardiac

arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdose. Potassium Iodide: Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing anginal pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdose. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

HOW SUPPLIED: Mudrane and Mudrane GG available in bottles of 100 and 1000 tablets; Mudrane-2 and Mudrane GG-2 in 100s; Elixir in pints and half-gallons.

Federal law prohibits dispensing without prescription.



WILLIAM P. POYTHRESS & COMPANY, INC., RICHMOND, VIRGINIA 23261

the sun and solar keratosis...

Over- exposed



and often underdiagnosed

Solar keratosis is not an uncommon medical problem.

Of course, the prevalence of keratotic lesions is greater in locations south of the 38th parallel—the so-called "Solar Keratosis Belt"—receiving the greatest amounts of solar radiation. However, solar keratosis can occur among any light-skinned population, usually in persons over 40, wherever people are subject to extended exposure to the sun.

Solar keratoses are generally not difficult to identify.

These skin lesions are usually multiple, flat or slightly elevated, brownish or red in color, papular, dry, rough, adherent and sharply defined. They are found on areas of the skin having extensive exposure to sunlight. Clinical characteristics of the lesions, their predominant location on exposed surfaces, the age of the patient and his skin type are important considerations in the diagnosis.

Solar keratoses can, and should, be treated because they are potentially premalignant.

Chronic exposure to sunlight frequently leads to degenerative changes in the skin. This can often result in the development of multiple, potentially premalignant keratotic lesions. Therefore, early detection and treatment is advisable.

Treatment with Efudex (fluorouracil) provides a high degree of effectiveness with a low recurrence rate, ease and convenience of therapy, low incidence of scarring, excellent cosmetic results in most cases, and a high level of patient acceptability.

Efudex[®] 5% Cream fluorouracil / Roche[®]

Because there may be more than meets the eye.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to

respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dis-

pensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris (hydroxymethyl) aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

(Editorials, continued)

Priorities

Environmentalists, Environmental Protection Authorities, hard starting but purer cars, the bandwagon news media, and common sense have made most all of us aware of the threatened contamination of our "planet earth." One of the chief victims of these opprobria has been DDT, which has adversely affected our woodlands, marshlands and fish population, but which is relatively safe to human beings.

These same forces have not mentioned the backlash to the banning of DDT. But

it appears that a significant amount of human illness has been caused in South Carolina by the use of pesticides alternate to DDT. According to the two reports on pesticide poisoning in this issue of JSCMA, it appears that about 1755 patients were treated for pesticide poisoning with 117 hospitalized, mostly requiring intensive care in the two year period 1971-1973. Is it better to poison people than the environment? I don't know. It seems there are no simple decisions anymore.

EEK

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We have DISPLAYED at every S. C. State Medical Society Meeting since 1921, and advertised CONTINUOUSLY in the S. C. Journal since January 1920 issue.

GENERAL PRACTICE REVIEW COURSE

September 7-13, 1975

The Board Examinations of the American Academy of Family Physicians will be given November 1-2, 1975. Therefore, The Division of Continuing Education of the Medical University of South Carolina will offer again the Sixth Annual Family Practice Refresher Course for those who may have missed it in February or who may wish to attend again. Thirty-eight and one-half (38½) AAFP credit hours will be given for attendance at this course. Lectures will be presented at the Mills Hyatt House Hotel with visits to various units of the Medical University complex for tours and demonstrations. The dates for this repeat course are September 7-13, 1975.

Registration is open now through Au-

gust 25, 1975. Enrollment is limited to 75, and tuition is \$150.00 payable in advance on or before September 7, 1975. A block of rooms is being held at the Mills Hyatt House Hotel at special convention rates. The Social Hour and Banquet on Wednesday evening is included in this fee. Wives are cordially invited.

A registration desk will be open from 6:30 to 8:30 p.m., Sunday evening, September 7, in the Middleton Room on the first floor of the Mills Hyatt House Hotel for the convenience of those participants wishing to complete their registration at that time. Final registration will be in the pre-assembly area at 8:00 a.m., Monday, September 8.

Please detach and return

REGISTRATION

GENERAL PRACTICE REVIEW COURSE

September 7-13, 1975

NAME _____ TELEPHONE NUMBER _____

ADDRESS _____ ZIP CODE _____

_____ Enclosed is \$150.00 tuition fee for General Practice Review Course

_____ Please send me hotel reservation card for Mills Hyatt House

_____ I plan to attend Social Hour and Banquet Wednesday evening

_____ My wife will also attend Social Hour and Banquet

Please make check payable to: Division of Continuing Education, MUSC, and mail to Dr. Vince Moseley, Director, Division of Continuing Education, Medical University of South Carolina, 80 Barre Street, Charleston, S. C. 29401.

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Medical University of South Carolina

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DRUG INFORMATION 8 a.m.-5 p.m., Mon. Fri. 792-3896

Rondomycin (methacycline HCl)

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines.

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to age 8 years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.** Usage in pregnancy. (See above **WARNINGS** about use during tooth development.)

Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in bone growth rate observed in premature infants given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organism including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on a anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopical discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours 300 mg every 12 hours. Gonorrhea. In uncomplicated gonorrhea, when penicillin is contraindicated, "Rondomycin" (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule. 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams "Rondomycin" (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia 900 mg daily for six days.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

SUPPLIED: "Rondomycin" (methacycline HCl): 150 mg and 300 mg capsules; syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev. 6/78



WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512



When the focus is on bronchitis due to susceptible strains of *H. influenzae* and pneumococci*

Rondomycin[®] 300 mg.

[methacycline HCl] Capsules

Delivers from the very first dose:

Studies show that after the first dose serum levels rapidly rise above minimum *in vitro* inhibitory concentrations

*Since many strains are known to be resistant, routine sensitivity testing is recommended

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As a rule, only pain that requires morphine is beyond the scope of Empirin® Compound with Codeine No. 4. That's because it delivers a full grain of codeine. (In the preferred phosphate form.) Its antitussive action is particularly appreciated by patients with fractured ribs, and following chest or abdominal surgery. Its low addiction liability is a bonus for all patients who require potent analgesia.

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Most other kinds of lesser pain respond to Empirin Compound with Codeine No. 3—whether musculoskeletal, neurological, soft-tissue or visceral. One might say No. 3 is an "all-purpose" analgesic — not too little, not too much. Just right for your out-patients in these categories.



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No.3, codeine phosphate*(32.4 mg) gr ½ · No.4, codeine phosphate*(64.8 mg) gr 1

*Warning — may be habit-forming.

Each tablet also contains aspirin gr 3½, phenacetin gr 2½, caffeine gr ½.

PERFORMANCE. IT'S A MATTER OF RECORD.

- an unsurpassed record validated in several thousand clinical papers
- rarely interferes with mental acuity
- wide margin of safety



Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous

occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. *Oral—Adults:* Mild and moderate anxiety and tension, 5 to 10 mg *t.i.d.* or *q.i.d.*; severe states, 20 or 25 mg *t.i.d.* or *q.i.d.* *Geriatric patients:* 5 mg *b.i.d.* to *q.i.d.* (See Precautions.)

Supplied: Librium® (chlordiazepoxide HCl) Capsules, 5 mg, 10 mg and 25 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Libritabs® (chlordiazepoxide) Tablets, 5 mg, 10 mg and 25 mg—bottles of 100 and 500. With respect to clinical activity, capsules and tablets are indistinguishable.

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Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

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**IN PAINFUL
ACUTE
CYSTITIS***

*nonobstructed;
due to susceptible
organisms



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RELIEVE THE PAIN WHILE YOU ELIMINATE THE PATHOGENS.

FOR THE PAIN

- ☐ Early relief of painful symptoms such as burning and pain associated with urgency and frequency.

FOR THE PATHOGENS

- ☐ Effective control of susceptible pathogens such as *E. coli*, *Klebsiella-Aerobacter*, *Staph. au-*

reus, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

Appropriate antibacterial therapy: Up to 3 days therapy with Azo Gantrisin 4 to 6 tablets *Stat.*, then 2 tablets *q.i.d.*; then 11 days with Gantrisin (sulfisoxazole) may be considered.

AZO GANTRISIN®

(50 mg phenazopyridine HCl and 0.5 Gm sulfisoxazole)

Before prescribing, please consult complete product information, a summary of which follows.

Indications: In adults, urinary tract infections complicated by pain (primarily cystitis, pyelitis and pyelonephritis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies.

Important Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents including the sulfonamides. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses, 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period. Contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.

Warnings: Safe use in pregnancy has not been established. Teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* Agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia.

Allergic reactions: Erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis. *C.N.S. reactions:* Headache, periph-

eral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Usual adult dosage for acute, painful phase of urinary tract infections is 4 to 6 tablets initially, then 2 tablets four times daily for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment of the infection with Gantrisin (sulfisoxazole) may be considered.

Note: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine soon after ingestion.

How Supplied: Tablets, each containing 0.5 Gm sulfisoxazole and 50 mg phenazopyridine HCl —bottles of 100 and 500.

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Nutley, New Jersey 07110



THE JOURNAL

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OCT 7 1975

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ADJUSTMENT REACTION OF CHILDHOOD

MANAGEMENT OF ACUTE PSYCHOSIS

ABDOMINAL AORTIC ANEURYSMS

APPROACHES TO MARITAL DISCORDANCE

VOLUME 71

SEPTEMBER, 1975

NUMBER 9

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Both often



Predominant
psychoneurotic
anxiety

Associated
depressive
symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor

neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

OCT 7 1975

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent

in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated, as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An 11.5 dose added to the b.i.d. or t.i.d. treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.



Valium® (diazepam)

2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnant, lactating or women of child-bearing age, weigh potential benefits against possible hazards.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully the pharmacology of agents employed. Drugs such as phenothiazines, barbiturates, and alcohol potentiate other antipsychotics and potentiate action. Usual precautions indicated in patients severely depressed or with latent depression or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbance, stimulation have been reported. Should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long term therapy.

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**of colic, diarrhea
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i-Soyalac and regular Soyalac are palatable, readily digestible and assimilated. It simulates human milk in appearance, taste and texture. It is complete with vitamins and minerals. It is suitable for infants and children who are sensitive to or cannot tolerate cow's milk.

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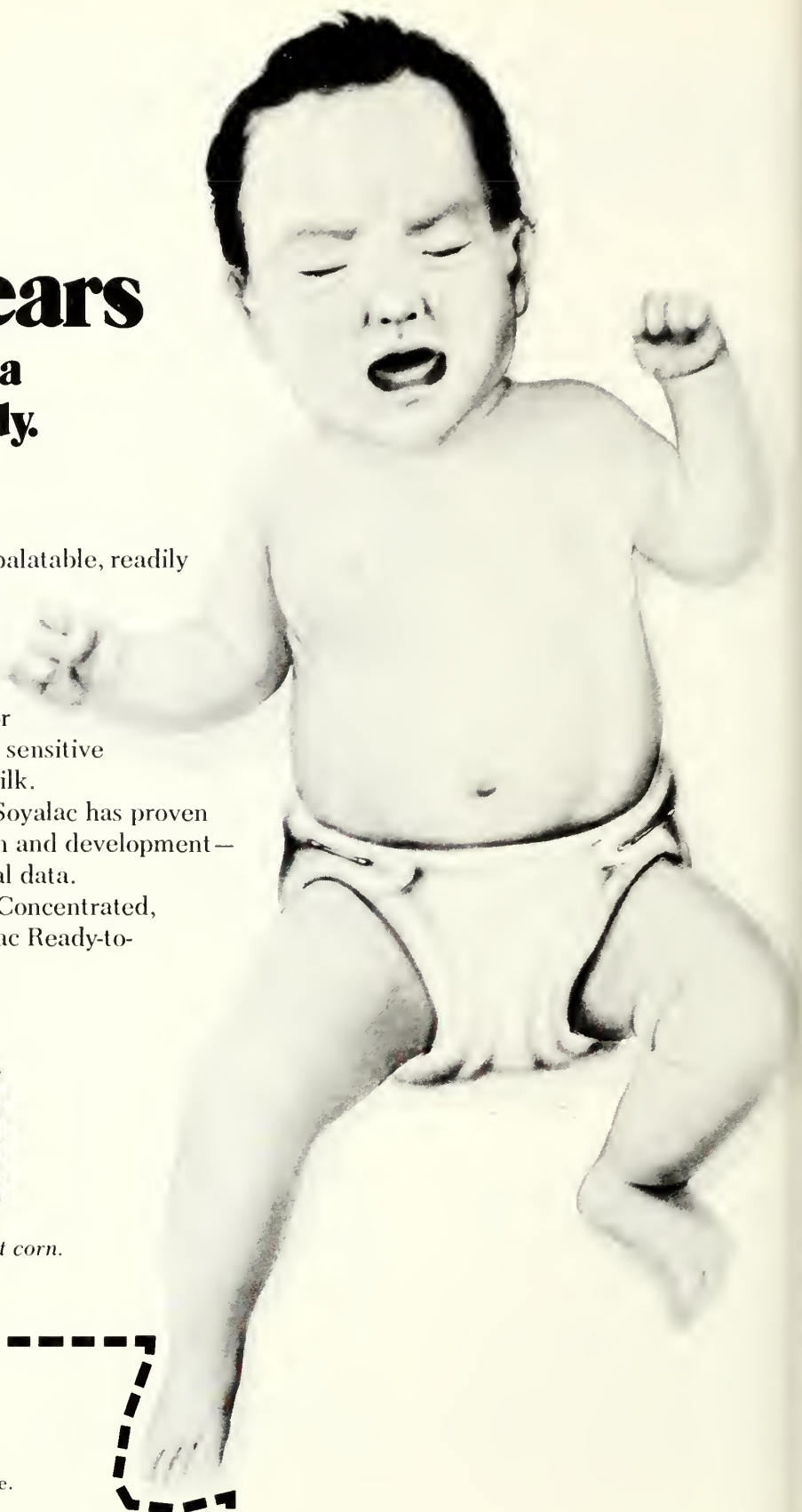
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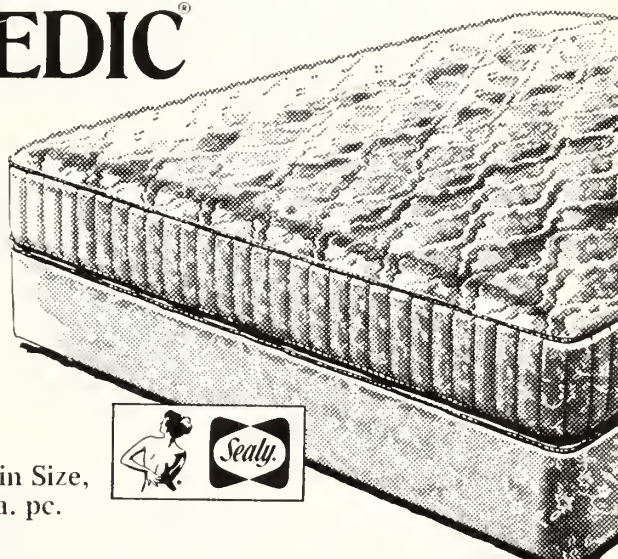
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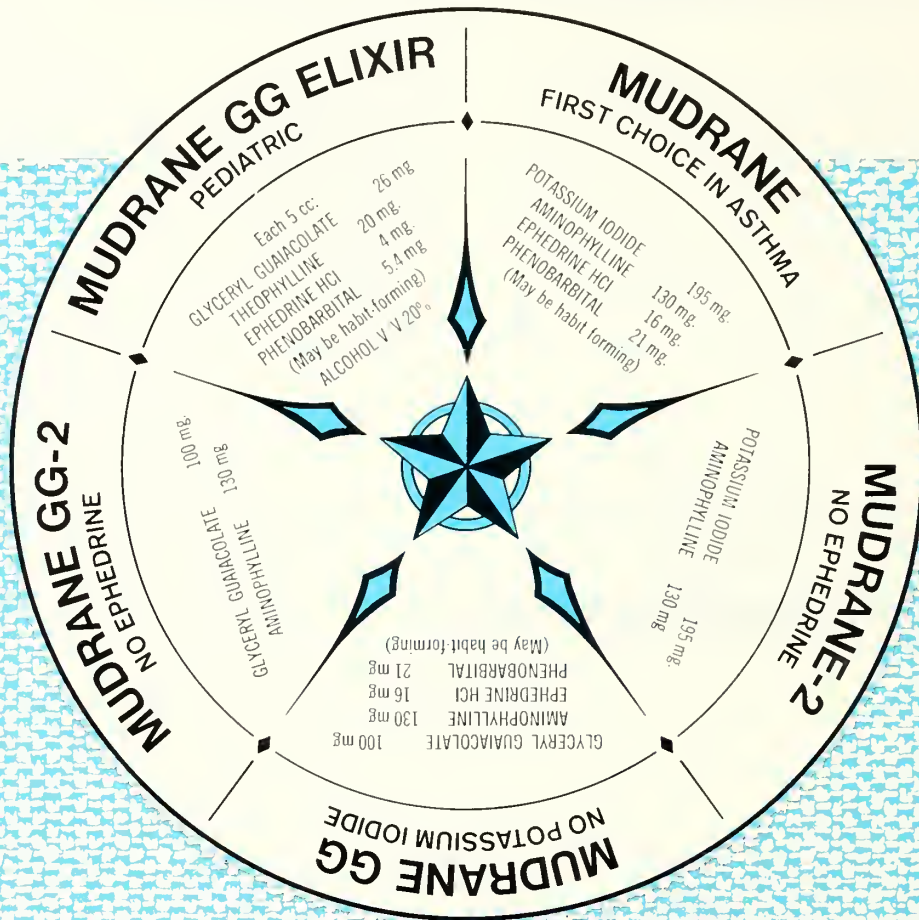
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STRESS AND MYOCARDIAL INFARCTION

C. WARREN IRVIN, JR., M. D.*
FRANK E. O'SHEAL, M. D.*

Matthew 6:27 And which of you by worrying and being anxious can add one unit of cubit to his stature or to the span of his life?

In a preliminary study of all patients admitted to a coronary-care unit during an eight week period, some preliminary conclusions regarding emotional stress were offered. It was felt in this small number of patients with acute myocardial infarction that emotional disturbance was an important factor. It also became evident that there was a high level of anxiety during the period of hospitalization which did not begin to resolve until after six months of recovery. Following the completion of this study, two of the authors decided to evaluate further the relationship of stress, primarily emotional, to myocardial infarction and also again to try to re-evaluate the amount and role of anxiety occurring during the acute phase as well as the convalescent phase. Some effort to evaluate the amelioration of symptoms with drugs was undertaken and a comparative study with Phenobarbital and Librium was included in the protocol.

The plan of the study was as follows: All the patients admitted to a coronary care unit by the Cardiologist (CWI) and who were felt to have a definite diagnosis

of an acute transmural myocardial infarction were taken in consecutive order and added to the study. All cases met the usual criteria of electrocardiogram and enzyme abnormalities. Any doubtful cases were eliminated as were those cases who did not survive long enough for initial studies to be carried out. A summary of the basic information is contained in Table 1. The plan of study was approved by the Institutional Research Review Committee. Each patient and family was informed as to the nature of the study and only one declined. Patient cooperation was overwhelmingly good. Each patient was then evaluated independently by both authors for evidence of anxiety, tension, anxiety-related apprehension and agitation while in the coronary care unit. These observations were repeated at the time of discharge from the hospital, at the end of the twelve weeks, at six months, and at one year. At these same time intervals the MMPI was administered to be used as a correlative measure for later evaluation. All MMPI's were administered by a single trained person who maintained control over the procedure.

In addition to this, ten parameters were evaluated independently by both physicians to determine the incidence of an abnormal or unusual amount of stress either just prior to or for a relatively long but

*Columbia, South Carolina

STRESS AND MYOCARDIAL INFARCTION

TABLE 1

50 Patients

Male 43 (38-69 yrs. — 154-212 lbs.)

Female 7 (35-63 yrs. — 130-150 lbs.)

Cigarettes	31
Pipe & Cigars (but no cigarettes)	8 (Eleven patients indicated significant change in smoking habits in past year.)
Alcohol	22
Diabetes	4
Hypertension	20
Adult Acquired Obesity	20
Previous myocardial infarction	2
Family history of myocardial infarction	24 (Parents-11, Siblings-7, Both-6)

definitive period before the myocardial infarction. These included job, wife, children, relatives, money, social position, lack of free time, environmental change, and "being a failure." In addition, #10 was unusual physical exertion.

The relationship of emotional stress to myocardial infarction has been discussed and evaluated for many years.^{2,3,4,5} On occasions, it seems the novelist* or the public has been more concerned over this problem than physicians, and professional interest has fluctuated rather markedly. Beginning with Flanders Dunbar⁶ in the early 40's and in the last 15 years most persistently by Friedman and Roseman^{7,4} numerous authors^{8,9,10,11} have contributed to the knowledge of this subject. Some of the material and the plan of this paper was taken from Jenkins' work of 1971.

An example of this waxing and waning of interest is exhibited in the program of the 49th Scientific Session of the American Heart Association in November of 1974 which, on a fairly close perusal, contains only one paper that is at all related to emotional factors and coronary disease.

An analysis of the results are as follows: Of the 50 cases evaluated regarding precipitating factors, in 13 of these no major stress factor was found by either of the two physicians, thus 26 per cent of our cases occurred in a setting in which no physical or emotional factor could be found relating either to the long-term development of the coronary disease or as an acute precipitating factor.

In the remaining 37 cases, at least one of the two physicians felt that there was a major emotional stress factor related to

*Two examples both from about two decades ago might be of interest to the reader. Those who have had an interest in evolution are aware of the famous Tennessee-Scopes trial of the first part of the 20th century. Mr. William Jennings Bryan is reported to have said that his and Mr. Darrow's courtroom conflict was "to the death." Although Mr. Bryan technically won the case, the victory was a Pyrrhic one. Mr. Bryan died suddenly three days after the trial of "acute indigestion." In the play "Inherit The Wind" the protagonist representing Mr. Bryan died in the courtroom at the conclusion of the trial ("Inherit The Wind," Jerome Lawrence and Robert E. Lee: Random House, September, 1955).

A paragraph from the novel Dr. Zhivago prepares the reader for Zhivago's death from myocardial infarction at an early age:

"Microscopic forms of cardiac hemorrhages have become very frequent in recent years.

They are not always fatal. Some people get over them. It's a typical modern disease. I think its causes are of a moral order. The great majority of us are required to live a life of constant, systematic duplicity. Your health is bound to be affected if, day after day, you say the opposite of what you feel, if you grovel before what you dislike and rejoice at what brings you nothing but misfortune. Our nervous system isn't just a fiction, it's a part of our physical body, and our soul exists in space and is inside us, like the teeth in our mouth. It can't be forever violated with impunity. I found it painful to listen to you, Innokentil, when you told us how you were re-educated and became mature in jail. It was like listening to a horse describing how it broke itself in" (Doctor Zhivago, Boris Pasternak: Pantheon Books, Inc., 1958, p. 483).

STRESS AND MYOCARDIAL INFARCTION

TABLE 2

	Non-Contributory			Moderate		Contributory Severe		Total	
	#	Psy.	Int.	Psy.	Int.	Psy.	Int.	Psy.	Int.
Job	1	26	28	15	7	9	15	24	22
Spouse	2	38	41	10	7	2	2	12	9
Children	3	33	37	12	6	5	7	12	9
Relatives	4	38	42	6	5	6	3	12	8
Money	5	36	40	10	6	4	4	14	10
Social Position "Pecking Order"	6	46	49	4	1	0	0	4	1
Lack of free time	7	34	37	7	12	9*	1*	16	13
Environmental Change	8	41	44	5	3	4	3	9	6
Being a Failure	9	28	45	12	4	10**	1**	22	5
Unusual physical exertion	10	42	43	7	7	1	0	8	7

N= 37 of 50 cases

*= p .05 and .01

**= p .01

(Environmental Stress Evaluations adapted from: Psychological and Social Precursors of Coronary Disease, C. David Jenkins, *The New England Journal of Medicine* 284 No. 5, Part 1, p. 244, Part 2, No. 6, p. 307, Feb 1971.)

the myocardial infarction. In 17 of these, both physicians agreed to the type and to the major degree of emotional stress. In 10 cases, one physician felt there was severe emotional stress, the other agreed there was emotional stress of the same type related to the incident, but did not agree this specific parameter or its severity was the most important stress factor. In one case, both physicians agreed there was severe emotional stress, but disagreed as to the parameter. In four cases, one physician felt there was major stress present in one parameter, the other physician felt there was some stress present in a different parameter. In five cases, there was disagreement between the two observers. It is of interest that in these five cases, the Psychiatrist felt that stress was present, but the Internist initially did not feel so. After the results were tabulated, these five cases were discussed in some detail.

The Internist agreed on re-evaluation that, certainly in three of the five, stress of some significant degree had been underestimated by him on his initial evaluation, but was clearly present. In two cases, there remains some disagreement. Table II shows the comparative evaluation to environmental stress.

In general, there is fairly good correlation between the Psychiatrist and the Internist although on some particulars, e.g., "lack of free time" and "sense of failure," the Internist seemed to rate this slightly higher than the Psychiatrist. In attempting to rectify these divergent opinions, it is evident that a specific qualifiable area of emotional stress is not always easy, and yet basic stress was well identified by the two physicians. Different emphasis on the outlined parameters may be explained by physician's bias secondary to training, type of practice, and

STRESS AND MYOCARDIAL INFARCTION

enculturation. The fact that the Psychiatrist was able to identify a somewhat greater number of stressful situations and to find a few more people with underlying deep-seated stress should not be surprising, even though specific effort was made by the Internist to uncover these problems.

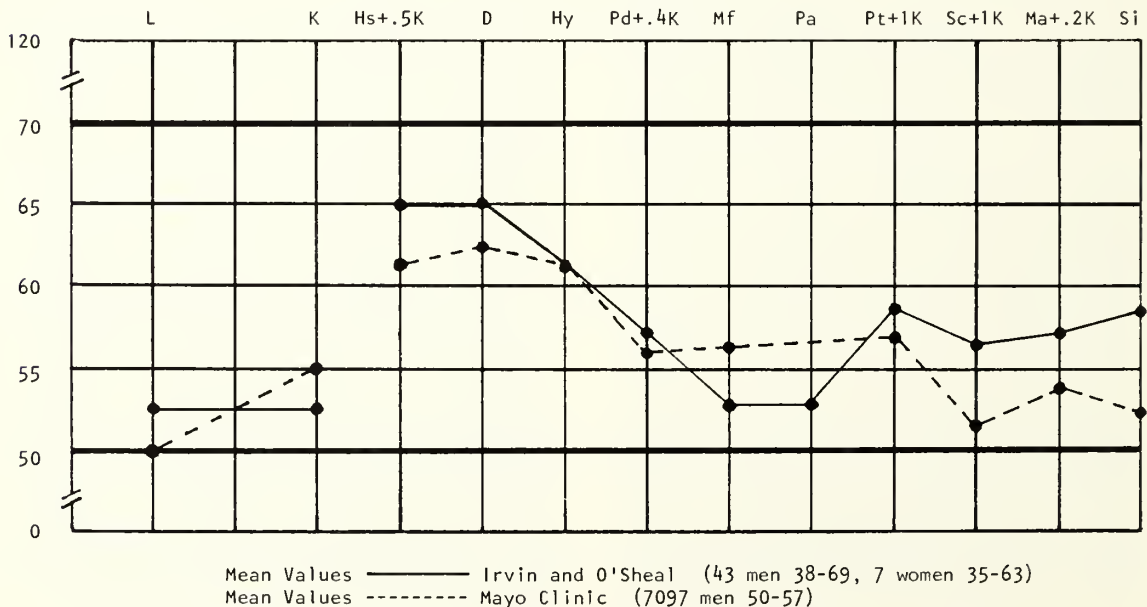
Only on one occasion did one of the physicians (the Psychiatrist) feel that severe physical exertion was present as a major cause of stress. The Internist did not agree because although the attack occurred at work on a hot, humid day, this was the normal, accustomed working pattern for this patient. They both agreed that there was some unusual physical exertion of some minor concern in seven cases. Recent report of "True" sudden death being related to physical exertion could help explain the lack of severe physical exertion as a precipitating episode in our cases.¹³

Our attempt to utilize the MMPI to corroborate our impression of increased anxieties at the time of admission and to help follow its course was unsuccessful. The follow-up results were conflicting both in relationship to personal evaluation and the relationship to the MMPI. We now feel a different approach will be necessary

to clarify this point and some of the impressions of our first report have not been confirmed. Certain facts did appear again. On the whole, the Psychiatrist evaluated the level of anxiety higher than the Internist, but more surprising to us was the failure of the anxiety, as represented by the MMPI especially, to decrease with time as had been demonstrated with the small number of cases in the initial study.

The MMPI also failed to demonstrate basic differences in personality patterns from the average. We were not too surprised that there was no difference from the normal regarding acute anxiety in the CCU as the MMPI is designed to show *traits* rather than any acute state. It is interesting, however, that the MMPI does not show any significant different pattern from the normal (Chart 1), thus failing to produce supporting evidence of personality differences such as Friedman's Type A and B but, equally obvious, it cannot exclude such differences either. Perhaps we can only say that at least in our hands MMPI can be safely and accurately done by acutely ill patients who are residing in rather stressful surroundings.

MMPI MEAN VALUES



STRESS AND MYOCARDIAL INFARCTION

Our results in regard to the drugs were of little help. No great difference could be determined by either author clinically, and statistical studies revealed nothing we could accept as an important improvement of one drug over the other.

In summary, our results confirmed our impression of a high level of emotional stress as a precipitating factor in the production of myocardial infarction. In 75 per cent of our cases the authors felt that a clearly demonstrable element of emotional stress preceded the infarction. Some of this stress was acute or abrupt, but with other patients the discomfort was more protracted. Many patients covered up their problems well, but when asked, seemed relieved and freely discussed their personal problems. The lack of a control group may make our results less valid to some. Our previous conclusions about decreasing anxiety, beginning six months after myocardial infarction have not been confirmed. Increased interest in uncovering anxiety remains an important aspect in the care of the patient

ill with acute myocardial infarction.

We frequently would be able to beneficially relieve a patient's anxiety about unfounded fears of his illness and the coronary care unit with a moderate expenditure of time and effort.

Both chemical and emotional supportive care is of benefit under these stressful situations. Effort by physicians along these lines will not only help relieve distressful anxiety in the hospital but will also help in returning a patient to a meaningful and productive quality of life. Further study of these most difficult aspects of an evidently multifactorial illness seem justified.

The authors wish to express our gratitude to the Hoffman-LaRoche Company for their support in this study. The help given by Mrs. Thelma P. Haley in giving the MMPI's, controlling the drugs, and keeping all the necessary records was a tedious task. We would not have been able to do the study without her, and we are extremely grateful.

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A BEHAVIORALLY ORIENTED PROGRAM FOR ADJUSTMENT REACTION OF CHILDHOOD

M. J. SHORT, M. D.***
THOMAS F. KIRBY, M. A.**
CLAUDE T. WILSON, M. A.*

A comprehensive treatment program for emotionally disturbed boys, ages 6 to 12, is provided by the Marshall I. Pickens Hospital (MIPH), a comprehensive community mental health center in Greenville, South Carolina. The Children's Program accepts emotionally disturbed patients from a variety of referral sources. The Program's philosophy is to involve the total environment of the child—his family, school, and community agencies—in the treatment process.

Children are referred for treatment by psychiatrists, pediatricians, psychologists, mental health centers, the school system, other agencies, and parents. Once a referral is made, a liaison therapist from the Children's Program works with the parents, the referral source, the school system, and other interested agencies in preparing a detailed history on the child for presentation to an Admissions Committee. This committee includes the Medical Director, the Director of the Children's Program, a consulting pediatrician and psychologist, and other staff members. After a review of the case, the committee decides upon the child's appropriateness for hospitalization. Table I reflects referrals and admissions from the program's inception through June, 1974.

***Medical Director, Marshall I. Pickens Hospital, P. O. Box 2758, Greenville, South Carolina 29602.

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*Director, Marshall I. Pickens Hospital Children's Program.

TABLE 1
REFERRALS AND ADMISSIONS
(April, 1969 - June, 1974)

<i>Description</i>	<i>Number</i>	<i>Percent</i>
Admitted	172	49
Waiting List	7	2
Applied - decision pending	5	1.5
Accepted - not admitted	20	6
Rejected	29	8
Referred - no application	117	33.5
TOTAL	350	100%

After the presentation and review, the Admissions Committee develops an initial treatment plan that specifies behavioral objectives, a complete physical by the consulting pediatrician, and an electroencephalogram and more extensive psychological evaluation as required.

In the Children's Program, the treatment plan is carried out by behavior therapists, trained in psychology and related fields. An educational program is also provided by the School District of Greenville County which furnishes two special education teachers, two aides, curriculum materials, and supplies.

Children arrive Sunday evening of each week. As an integral part of their treatment, they spend weekends at home where their behaviors are closely monitored by their parents. Weekend activities and any problematic behaviors are recorded in a diary by the parents, which is discussed on Sunday evening with a behavior therapist.

Children are grouped by age with the younger group being for ages 6 to 9 and

ADJUSTMENT REACTION OF CHILDHOOD

the older group for ages 10 to 12. Since many of their problems center around the school setting, they attend special classes six hours each day. Because most of them are at least one to two years behind in their school work, these classes are designed to provide individualized programs in the basic academic skills. Behavioral and emotional management in the classroom, as well as curriculum, is coordinated with the child's treatment program through periodic staff meetings involving the behavior therapists, special education teachers, and the director.

During the afternoon and evening, children participate in activities specifically designed to help overcome their emotional and behavioral problems. These activities are recreational in nature and include swimming, hiking, and both individual and competitive sports. Through these activities, each child learns that there is some area in which he can excel, that he can do some things which he was afraid to try, and, perhaps most important, that he feels better about himself for having participated. Of equal importance is the way in which the staff uses these normal childhood activities to work on the children's treatment goals. Many situations occur in a ballgame, for example, which require a child to develop temper control, cooperative behaviors, and other social skills necessary for normal adjustment.

For the overall treatment program, the behavior therapists have developed a token economy based on principles of operant conditioning. Patients earn either punches on their token cards (older children) or poker chips (younger children) for following the few basic rules of the program, progress on individual goals, completing school work, or exceptional performance in any area. The points are necessary for purchasing recess time during the school day and a variety of activities during the remainder of the day. On Friday, each group opens a community store where extra points can be spent for

toys.

In addition to the milieu concept of treatment, a child may also be involved in play therapy sessions, individual counseling, or family therapy. Nurses administer any medication that is involved in his treatment, and the Medical Director monitors the total treatment program.

The typical referral to the Children's Program is diagnosed as Adjustment Reaction of Childhood and may be characterized as follows: He is a ten year old boy who is having problems both at home and at school. At school he is often described as being hyperactive, getting very upset when told he is wrong, not obeying limits and failing to complete any classwork. At home he uses destructive acts to get attention, lies, throws temper tantrums, and is apt to run away.

In the home there is a great deal of friction between this boy and his siblings. Because of her husband's long hours at work the mother enforces most of the discipline. She is unable to deal with his behavior effectively and has become quite frustrated with their relationship. As a result, she typically responds to his problematic behavior by yelling and threatening, but rarely provides consistent consequences for his behavior.

While in the first grade, this boy was very active, somewhat rebellious, and made only average grades. His later academic grades demonstrated a gradual deterioration and increased behavioral and academic deficiencies were reported. Frequently he has been prescribed a variety of tranquilizers and/or psychostimulants. These trials on medication have been of little benefit.

These families represent all income levels (Table II). Educational levels vary considerably with 38 percent of the parents being high school graduates, 10 percent having had some college, and 10 percent being college graduates. In family composition, 54 percent of the patients are living with both natural parents with the next largest group, 17 percent, living with

ADJUSTMENT REACTION OF CHILDHOOD

TABLE II
LEVELS OF GROSS FAMILY INCOME

<i>Income Level</i>	<i>Number of Families</i>	<i>Per Cent</i>
Below \$4,000	28	17
\$4,000 - \$6,999	26	15
\$7,000 - \$9,999	39	23
\$10,000 - \$12,999	26	15
\$13,000 - \$15,999	25	15
Above \$16,000	26	15
TOTAL	170	100%

TABLE III
SIBLINGS POSITION OF PATIENTS

<i>Description</i>	<i>Number</i>	<i>Percent</i>
Only	17	10
Oldest	47	28
Middle	26	16
Youngest	54	32
Next Oldest	14	8
Next Youngest	10	6
TOTAL	168	100%

only their natural mother. The sibling position of patients is shown in Table III.

A fundamental and essential segment of the Children's Program is the Child Management Workshop which all parents must complete as a prerequisite for the child's admission. The Program's philosophy necessitates direct parental involvement in the child's treatment, therefore, a contractual agreement between the parents and the Program specifies parental participation in a parent training group and/or individual counseling. The Child Management Workshop focuses on principles of behavior management, parent training, and family relationships. These sessions serve to prepare the parents to work effectively with their child's treatment team. After completion of the Workshop, all parents meet periodically with team members for management counseling and to review their child's progress. The intent of the Workshop and counseling sessions is to assist each parent in becoming more effective in dealing with his or her child.

After an average length of stay of 6 months, most of the children return to a regular classroom (Table IV). One month

prior to the discharge date, a liaison therapist visits the school to talk with the principal about placement and the choice of a teacher. A joint conference between the selected teacher, principal, and liaison therapist is then arranged, as well as a time for the child to visit the school. If there is any question as to how the child will adjust to the regular classroom, the child may attend the class and return to the Children's Program in the evening for a few days. Following discharge the liaison therapist maintains contact with the school and family for one year. If needed, consultation and support is continued beyond the one year.

In addition to the normal follow-up, all discharged patients are eligible to participate in an Aftercare program, referred to as Alumni meetings. The objectives of this service are to maintain gains made during treatment and to provide support as the children readjust to their community. Held every third week by a liaison therapist and behavior therapist, the Aftercare activities include group counseling and recreational activities. Counseling focuses on any problems in readjustment the children may be experiencing either at home or at school.

Thus far children have participated in the Aftercare program from 6 to 12 months following their discharge. Follow-up records indicate that approximately 82 percent are functioning satisfactorily in their home and school relationships. Eighteen percent were unable to function satisfactorily in the regular classroom, at home, or both.

TABLE IV
DISCHARGE PLACEMENT
(April, 1969 - June, 1974)

<i>Placement</i>	<i>Number</i>	<i>Per Cent</i>
Regular Classroom	133	89
Special Education		
Classroom	8	5
Military School	2	1.5
Whitten Village	2	1.5
Not in School	3	2
Deceased	1	1
TOTAL	149	100%

ADJUSTMENT REACTION OF CHILDHOOD

After five years of operation the MIPH Children's Program has developed a comprehensive treatment program for children. The strength of the Program lies in its flexibility which allows adaptation to the needs of the community and population served, and in its inter-disciplinary base for prescribing and evaluating the

various treatment programs. Follow-up records indicate that the vast majority of the children treated are now functioning satisfactorily in both their home and school. A formal follow-up study is now being conducted and will be reported at a later date.

THE MEDICAL-PHARMACOLOGICAL MANAGEMENT OF ACUTE PSYCHOSES

LAURENS D. YOUNG, M.D.*

The patient who presents in an acute psychotic state can pose a vexing problem for the primary physician, who must contend not only with the management of the individual himself, but often with a family pleading for help, and occasionally with hospital or community agency staff who are upset and confused by the disturbed patient's behavior. In such cases, immediate psychiatric referral would obviously be ideal; however, in areas without ready access to a psychiatrist or qualified psychiatric facilities, such a disposition may take an agonizingly long time. Familiarity with some of the newer methods of psychiatric medical management can allow the primary physician to provide prompt, decisive palliative care which can meet the needs of the patient and those around him safely until more comprehensive psychiatric care can be arranged.

This paper will present the essentials of recognition and management of psychotic behavior in combination with some of the newer (primarily chemical) approaches to the psychotic patient which can be utilized with some efficacy in a general hospital setting. A critical period of 72 hours has been chosen as a focus. Hopefully, specialized psychiatric care can be arranged during this time. Of course, such cases are probably rare among the wide range of psychiatric problems which present in a primary practice, but the intensity of the problems raised by the rare acute psychosis seems to demand some special attention.

DIAGNOSIS

As in all medical treatment, a proper diagnosis—in this case the recognition of

psychosis—provides the key to proper management. Some familiarity with the DSM-I or DSM-II¹ nosology taught in medical school is helpful, but a detailed diagnosis and psychological formulation are not necessary to initiate care for the psychotic individual. Presumably the physician has already been able to rule out and treat appropriately the acute medical, surgical, and neurological syndromes which can present with a psychosis.

Although psychotic symptoms are commonly thought of as arising in persons who are schizophrenic, dramatic symptoms of psychosis can occur in other disease states such as the affective disorders (the manias and depressions), the brain syndrome of aging, and secondary to "benign turmoil" or drug-taking in adolescence, as well as the schizophrenic and paranoid conditions. Often, especially in young people, a combination of etiologies can be presumed, and very often the precise diagnosis cannot be made even with resolution of the psychosis. On the basis of symptoms alone, differentiation of acute manic states from acute schizophrenic reactions is extremely difficult even for experienced psychiatrists.² In practice other factors such as age, sex, history of drug use, family history, and previous knowledge of the patient often provide better clues to diagnosis than signs and symptoms,³ but *on the basis of symptoms alone an impression of an acute psychotic state can be formed and treatment initiated.*

Psychosis implies a disruption of personality severe enough that the patient is unable to carry out the ordinary activities of daily living.⁴ In the severest form this can mean a disturbance of eating, sleeping, and the ability to use language

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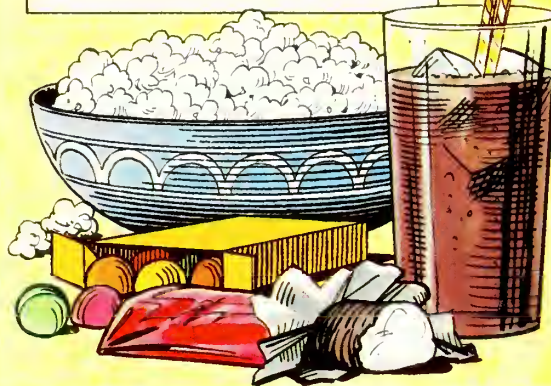


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effectively. In some obvious cases the patient may have hallucinations or delusions. In less obvious cases a psychosis can be recognized by the characteristic difficulties in attention and span of thought. The patient will be unable to maintain a conversation for an extended period. He may stop in mid-sentence, become mute, or answer questions in bizarre or illogical ways. He may skip from one subject to another in a manner which seems illogical. Instead of attempting to communicate in normal speech, he may substitute body language, staring, or use foreign words. The patient's affect may appear flattened, extremely excited, depressed, or even angry or frightened, but will probably be incongruent with his apparent condition. Such a patient can be thought of as disorganized in the social and emotional sense.⁵ The patient with this degree of disorganization of thought processes and its consequent effect on his ability to function is psychotic and requires treatment.

ADMISSION TO THE HOSPITAL WARD

The patient should be admitted to a suitable hospital setting. A general ward with private room facilities and the availability of at least one nursing staff person with some experience in the care of psychiatric patients who can attend the patient during the initial steps of treatment are highly desirable and probably essential. A private-duty nurse may be helpful, provided she has some experience and competence with psychiatric problems. Family members and friends should not visit until the psychosis has subsided somewhat. Most families and friends will have spent enough time with the patient during the earlier phase of his psychosis to be quite willing to take advantage of the relief which hospital care affords.

In general, the presence of a confident and non-threatening staff member for 15 to 30 minutes every hour combined with rapid tranquilization (as described below) should be sufficient to assure the patient

that he is being properly attended.⁶ Physical restraint or isolation in a stripped room for very brief periods (30 to 60 minutes) may be useful to help the patient through periods of extreme agitation when there is danger that he may harm himself. If such measures fail after a few hours, the patient may not be sufficiently cooperative to allow safe care in a general hospital. This discussion cannot include treatment of the very uncooperative, belligerent or dangerous person who will require police intervention and perhaps civil commitment for proper care to be given.⁶

Once the patient is admitted to the hospital, care should be taken to establish as complete a history of previous medications as possible. This can often be obtained from a relative or close friend rather than from the patient. Helpful information includes previous diagnosis, hospitalization, type of medication used, and the patient's responses to it. Especially important is a record of any allergies or sensitivities to medication. A family history of psychiatric diagnosis or responses to medication can also aid the physician in his choice of treatment.

Rapid tranquilization^{7,8} is a treatment method which allows rapid control of an acute psychosis by administration of relatively high doses of the newer antipsychotic compounds in a relatively brief period of time (72 hours in our case). Ideally, within the first 24 hours a level is reached at which the patient is able to sleep for short periods of time, has some lessening of his fright, anger, and agitation, and gains some ability to think and communicate in a more organized fashion. In the next 48 hours adjustments to this level of medication are made in order to maintain or possibly improve the patient's mental state.

The object of rapid tranquilization is to build up a therapeutic drug level in the patient without "snowing" him, that is, sedating him so severely that he sleeps for several hours, making his symptoms non-

The initial therapeutic dose should be estimated by the severity of the symptoms and the size of the patient. Initially, an oral dose of chlorpromazine, 200-400 mg. (in liquid form, if possible), should be given. This is a rough estimate because it has been found that plasma chlorpromazine levels can vary tremendously between patients.¹⁰ Occasionally a slight woman may require more medication than a husky, young football player with a similar degree of psychotic symptomatology. As a rule, chlorpromazine, 200-400 mg., provides a dose range which should have at least a significant effect on any psychosis, but will not be sufficient to "snow" the patient. A dose of this size would, however, almost surely be profoundly sedating for a non-psychotic person.

After 2 hours of observation, a second oral dose of chlorpromazine can be given. This dose should be 100-200 mg., depending on the amount of sedation observed and the therapeutic effect of the previous dose. A 2-hour time-period is chosen because the sedative effect should be reaching its peak and this allows the physician to weigh the increasing sedation against the therapeutic effects (increased ability to communicate effectively, reduction in agitation, appropriateness of affect, and so on). In another 2 hours the same observations and judgments can be repeated and another dose in the range of 100-200 mg. selected. This process of observation and administration can be repeated every 2 hours until the desired effect is achieved.

If parenteral medication is necessary, the IM dose should be half of the planned oral dose. Not more than 100 mg. of chlorpromazine can be given IM. If IM medication is necessary, the time of observation can be shortened to 1 hour after the last injection. This is usually effective and safe because both the therapeutic and sedative effects are somewhat more rapid with IM medication. Note that the total rate of administered medication does not change when using medication in this way. None of these medications should be

given intravenously.

In a few hours a relatively high level of drug can be administered with careful consideration of the increase in the most common side-effects. The method of administering chlorpromazine in this manner is outlined in figure 2. When the proper balance of antipsychotic control versus sedation has been achieved on day 1, the next day's dose will be approximately two-thirds of the total oral and IM dosage of the first day on a b.i.d. or t.i.d. schedule. The third day's dosage will be similar to the second day's with minor adjustments.

The patient should be observed for the effects of medication every 15 minutes for the first 2 hours. Blood pressure should then be taken at least every half-hour. Blood pressure drops of 0-20 mmHg are very common. Blood pressure drops of more than 20 mmHg are not uncommon and should be treated by having the patient lie supine for long periods with instructions to arise slowly, if he must arise. Blood pressure drops greater than 40 mmHg are almost always symptomatic and call for change to a drug less likely to cause such side-effects.

RAPID TRANQUILIZATION WITH NON-SEDATIVE DRUGS: HALOPERIDOL

In the case of haloperidol, extrapyramidal effects, rather than sedation and hypotension, are the main problems with rapid administration and high doses. This medication has the advantage of more rapid administration because the possibility of oversedating the patient is much less than with chlorpromazine. Therefore, the interval between doses can be shortened to 1 hour. The main obstacle to rapid tranquilization is the frequent occurrence of extrapyramidal symptoms which require control with additional, anti-Parkinson medication. This drug is usually preferred for the patient with less agitation and greater degrees of thought disorder than those treated with chlorpromazine. This method is dia-

MANAGEMENT OF ACUTE PSYCHOSIS

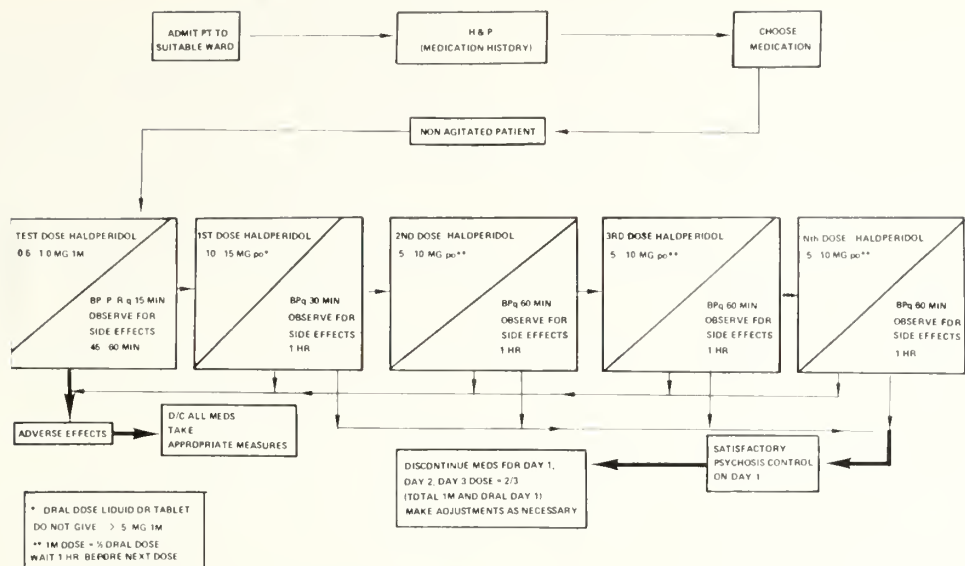


Figure 3. Schematic diagram of suggested method for rapid control of psychosis using Haloperidol.

grammed in figure 3.

An initial dose of Haldol, 10-20 mg. PO, can be given with the exact size of the dose dependent on patient size and symptoms, as with chlorpromazine. A dose of 5-10 mg. can then be repeated every hour, depending upon the balance of therapeutic effect and side-effects. A total up to 100 mg of Haldol may be given in 24 hours. Control of acute psychotic symptoms can frequently be obtained with 40-60 mg. It is not usually necessary to halve the oral dose if IM medication is given: 5-10 mg. may be given IM. As with oral medication, 1 hour is an optimum time to observe the patient for therapeutic and side-effects before deciding on the need and size of subsequent doses.

As with Thorazine, the next 48 hours' medication can be estimated from the first day's dosage by calculating two-thirds of the total IM and oral medication of day 1 and placing the patient on a t.i.d. schedule. The dosage of days 2 and 3 will be similar with only minor adjustments. The object is to maintain or somewhat improve the therapeutic level of the previous day, so slight adjustments of medication may be necessary.

Extrapyramidal side-effects occur in something over 50 per cent of acutely

psychotic cases treated with Haldol and the proportion is almost surely higher in cases treated with high, frequent doses of Haldol. The dyskinesias, dystonias, and pseudo-Parkinsonian symptoms are easily recognized by the primary physician. The symptom of this drug most difficult to recognize is akathisia, which is a motor restlessness, usually in the lower extremities, often accompanied by a leg tremor or tapping of the feet. Akathisia is often described by the patient as an "inability to sit still."

The recognition of any EPS calls for the institution of standard anti-Parkinson therapy. A daily dose of benztrapine (Cogentin, Merck), 1-6 mg. PO, or trihexyphenidyl (Artane, Lederle) 2-12 mg. PO, in a divided dosage schedule of b.i.d. is usually sufficient. The approximate daily dose necessary can be estimated by using a ratio of 1 mg. Cogentin or 2 mg. Artane for each 200 mg. Thorazine or 4 mg. Haldol. It is best not to exceed the maximum recommended daily dose of anti-Parkinsonian drugs because of the strong anticholinergic effects of these drugs (dry mouth, increased pulse rate, blurred vision, constipation, and urinary difficulties); such effects are common with the antipsychotic drugs and can be

worsened by anti-Parkinson drugs. There is also a minor danger of increasing the severity of a psychosis (the "central anticholinergic syndrome") with these drugs.²⁰ For particularly acute disturbing symptoms such as oculogyric crisis or spasmodic torticollis, benztropine (Cogentin), 1 mg., may be given either intramuscularly or intravenously for especially fast relief. Dephenhydramine (Benadryl), 50-100 mg. IV, should also relieve a very disturbing and painful side effect within 1 or 2 minutes.

In general, a relatively low dose of anti-Parkinsonian medication given orally twice daily is sufficient to control EPS. Should parenteral medication be necessary for particularly disturbing side-effects more than once, the antipsychotic medication should be discontinued and a medication less likely to produce these side-effects should be substituted. In any case, the anti-Parkinson medication should be continued orally for 4-6 weeks once it has been initiated, and for 2-3 days after the antipsychotic drugs have been terminated. Although it is beyond the focus of this paper, the EPS have been found to be transient in 90 per cent of cases,²¹ and in most cases the anti-Parkinson medication can be discontinued even with chronic

use of antipsychotics.

In spite of the drama that surrounds them, most acute psychotic states can be managed in a rational medical manner once they are recognized. Admission to a hospital ward where the psychotic patient can be treated confidently and safely is essential. The choice of a drug depends upon the spectrum of side-effects it produces, the patient's ability to tolerate them, and the physician's ability to recognize and remedy the various effects. In general, agitated patients have been treated with the sedative type of drug and less excited patients with the non-sedative drugs. Either a sedative or non-sedative drug can be titrated effectively and safely for any psychosis, using the rapid tranquilization protocol. The main side-effect of the sedative drugs, hypotension, and the main side-effects of the non-sedative drugs, extrapyramidal symptoms, can be recognized and treated safely using this method. Such adverse effects should not present an obstacle to therapy in the first 72 hours. A 3-day period of rapid tranquilization should allow the patient to be competently managed until more comprehensive psychiatric care can be arranged.

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TREATMENT OF ABDOMINAL AORTIC ANEURYSMS

R. RANDOLPH BRADHAM, M. D.*

The definitive treatment for an abdominal aortic aneurysm is resection and replacement with a prothetic graft. This is an imposing procedure for a patient in spite of the marked improvement in techniques, grafts, and supportive care. The operative mortality has declined steadily and the contraindications have narrowed. There remains, however, a group of patients for whom this operation is too hazardous. For many patients, judgment for operation is easily made, but for others this decision is the most critical factor in their management. Usually, the aneurysm is only part of a degenerating vascular system that might have already attenuated vital organ function. Many patients with aneurysms are in the eighth and ninth decades and have a short life expectancy.

It is the purpose herein to review the indications and contraindications for operative repair, to present a modest series of patients treated operatively, and to outline management based on the experience gained from this group of patients.

SYMPTOMS

Most aneurysms are asymptomatic. Many are found on routine examination or on roentgenograms of the abdomen made for the purpose of studying some other organ such as the stomach, colon, or kidneys. A few cause significant back pain, presumably due to irritation on the spine and its coverings. Dissection or rapid expansion may cause moderate to severe pain. Sudden abdominal pain in a person known to have an aneurysm especially when associated with hypotension, is indicative of leaking of the aneurysm.

INDICATIONS AND CONTRAINDICATIONS

The size of an aneurysm would serve some basis for selecting patients for opera-

tion provided there are no other contraindications. It is difficult to pick a certain size below which a patient would be safe and above which he would be in danger. A good "ball park" figure would be 5 cm in diameter. Small aneurysms will rupture, but certainly the incidence is much lower than with the larger aneurysms. One important factor is the rapidity with which an aneurysm is expanding. Perceptible increases in size between periodic examinations would be a strong indication for operation. Resection of a small aneurysm in a fifty-five year old patient who is in fairly good health would be reasonable, whereas, a seventy-eight year old patient with a small aneurysm and heart disease, might fare better if kept under observation.

In an outstanding article on this subject by Szilagyi, Elliott, and Smith,⁶ the contraindications for operation on asymptomatic patients were given as follows:

1. acute myocardial infarction of less than three months' standing
2. intractable congestive cardiac failure
3. intractable angina pectoris
4. severe pulmonary insufficiency (dyspnea at rest)
5. incapacitating residuals from cerebrovascular thrombosis or hemorrhage
6. renal functional impairment resulting in a serum creatinine level of 3.0 mgm/100 ml or more
7. associated lethal disease with less than three years' survival expectancy
8. small size of aneurysm (less than 6 cm in diameter) in a patient seventy-five years of age
9. advanced age (greater than 80 years, insofar as possible physiologically defined)

These criteria are helpful in the in-

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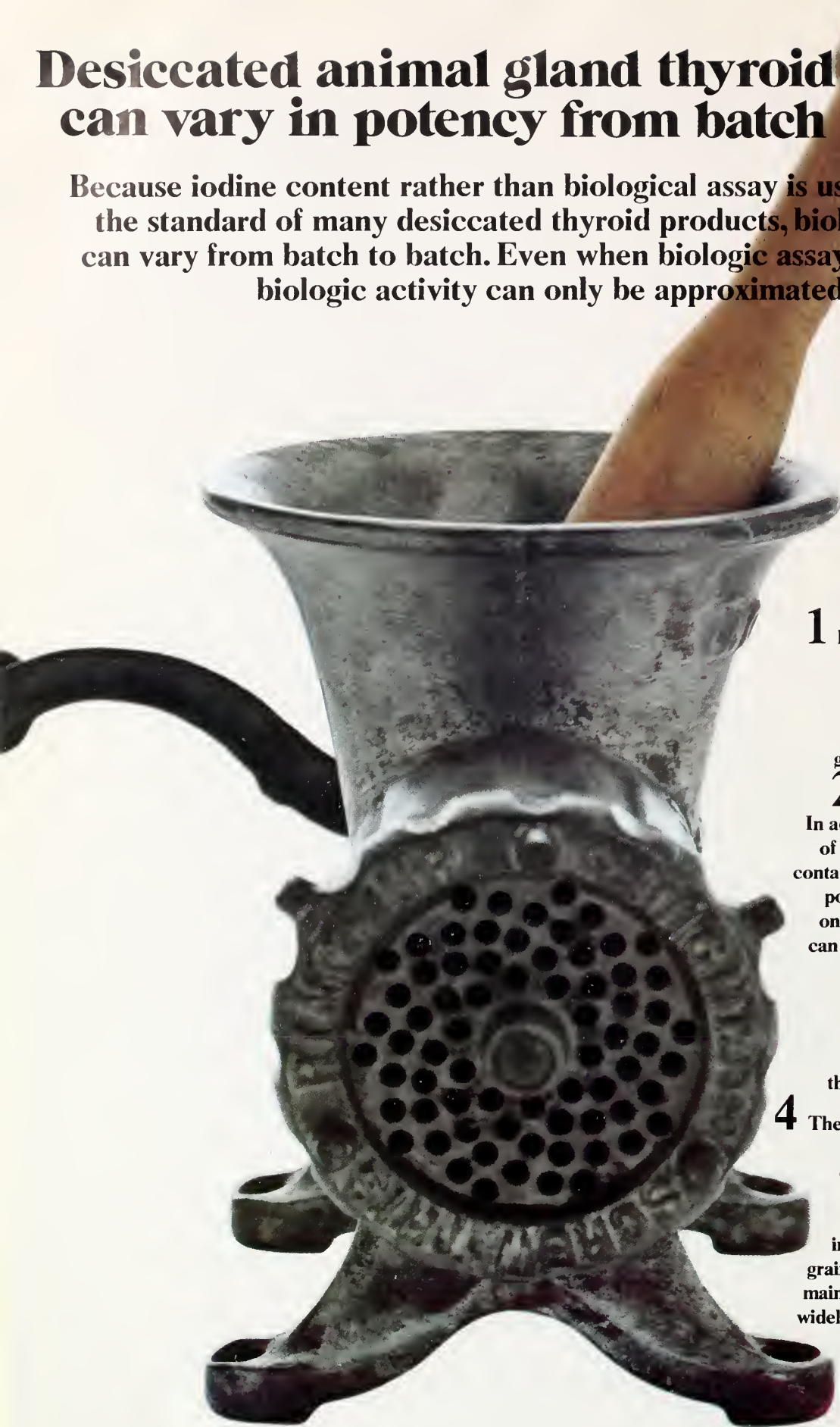
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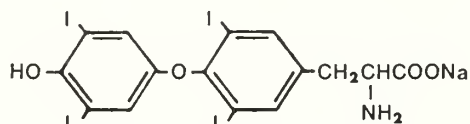
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Contraindications

There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis. (See WARNINGS)

Warnings

Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions

Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule. With SYNTHROID (sodium levothyroxine) Tablets, the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

Adverse reactions

Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration

For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0.2 mg) of SYNTHROID (sodium levothyroxine) Tablets daily will restore normal thyroid function and only occasionally will patients require larger doses. Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism, special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent onset of hypothyroidism, full replacement dose of 150 mcg (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view of the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patient as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedematous infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 mcg (0.025 mg) per day. Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at three to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration.

Laboratory tests to monitor thyroid replacement therapy are of limited value. Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with the clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occurs and should not be considered evidence of overdosage per se.

In all cases, clinical impression of the well-being of the patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critical importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size, the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROID Injection may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsiveness within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred. Like the oral dosage form, SYNTHROID Injection produces a predictable increase in the circulating level of hormone with a long half-life. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient is fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

SYNTHROID Injection by intravenous or intramuscular routes can be substituted for the oral dosage form when ingestion of SYNTHROID Tablets is precluded for long periods of time.

How supplied

SYNTHROID (sodium levothyroxine) Tablets are supplied as scored, color-coded compressed tablets in 6 concentrations: 25 mcg (0.025 mg)—orange . . . 50 mcg (0.05 mg)—white . . . 100 mcg (0.1 mg)—yellow . . . 150 mcg (0.15 mg)—violet . . . 200 mcg (0.2 mg)—pink . . . 300 mcg (0.3 mg)—green. Depending on strength, these tablets are available in bottles of 100, 500, 1000 and 5000.

SYNTHROID (sodium levothyroxine) for Injection is supplied in 10 ml vials containing 500 mcg of lyophilized active ingredient and 10 mg of Mannitol, U.S.P. A separate 5 ml vial containing Sodium Chloride Injection, U.S.P. is provided as a diluent.

Directions for reconstitution

Reconstitute the lyophilized sodium levothyroxine by aseptically adding 5 ml of the Sodium Chloride Injection, U.S.P. to the vial. Shake vial to insure complete mixing. Use immediately after reconstitution. Discard any unused portion.



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*U.S. Pat. 2,889,363

ABDOMINAL AORTIC ANEURYSMS

dividual consideration of a patient for operation. There are no contraindications to operation on a patient with a ruptured or rapidly expanding aneurysm. Kraft,³ using similar criteria, is following 131 patients with abdominal aortic aneurysms. Fifty-six have been followed for five or more years. This represents approximately 25 per cent of the aneurysm population treated by his group.

CLINICAL EVALUATION

All patients with abdominal aortic aneurysms for whom operation is contemplated are admitted to the hospital for a complete evaluation. A chest film, EKG, blood chemistry determinations, pyelograms, and evaluation of clotting factors are done routinely. Pulmonary function studies, urinary excretion evaluation, and a glucose tolerance test are done when indicated. Usually, a cardiologist or internist is asked to help evaluate the patient and to follow them throughout their course.

Aortography is now done almost routinely. Although the diagnosis has been established by palpation and abdominal roentgenograms, the aortogram adds much valuable information related to size and extent of the aneurysm, relationship of the aneurysm to the renal arteries, and the condition of the run-off vessels (Figures 1-5).

CLINICAL SERIES

Forty patients having abdominal aneurysms have been operated upon by the author during the past seven years. Thirty-five patients were operated upon whose aneurysms had not ruptured. Five patients were operated upon who were admitted with a ruptured aneurysm. There were two deaths in the group without rupture and two deaths in the group of five patients whose aneurysms had ruptured prior to admission.

The two patients who died with ruptured aneurysms were both moribund on admission and operation was done only as a desperate attempt to resuscitate the patients. One of the patients having an elective operation developed a fistula between the upper anastomosis and the duo-

denum. Reoperation and insertion of another graft was done, but he eventually died of sepsis. The other patient who died was actually admitted for evaluation of a lung density consistent with carcinoma. During the evaluation, a large aneurysm was found and the patient developed abdominal pain. Decision was made to resect the aneurysm first as it was more life threatening. On the second postoperative day, the patient developed bradycardia at a rate of 32/minute and A-V dissociation. He died shortly thereafter, presumably from a myocardial infarction. Autopsy was not granted.

COMPLICATIONS

One patient developed chylous ascites requiring operation six weeks later because of continuing protein loss. Multiple leaks in the lymphatic channels at the level of the upper anastomosis were sutured and the patient had no further trouble. This case was reported by Bradham and Gregorie² as chylous ascites postoperative resection of an abdominal aortic aneurysm had not been recorded in the literature at that time.

One patient was operated upon because of postoperative hemorrhage. A small hole was found in the wall of the left renal vein which was actively bleeding. It was believed that it was a defect created when a small branch had been sheared away. Simple suture closed this defect. One patient developed an obstruction of the left femoral artery on the first postoperative day. Thrombectomy was done and flow re-established.

Complete thrombosis extending down into the iliac arteries occurred in one patient who had a straight graft inserted. This was removed and a bifurcation graft to the femoral arteries was used to replace it. In all probability, sluggish flow through diseased and partially occluded iliac arteries caused the graft thrombosis.

Two patients developed delirium tremens but responded well to sedation and supportive care. Two other patients developed congestive heart failure. Both

ABDOMINAL AORTIC ANEURYSMS



Figure 1. Aortogram showing large aneurysm with adequate cuff between renal arteries and aneurysm. Because of size of aneurysm, this could not be determined by palpation.



Figure 3. Small aneurysm, but with small bulge which at operation was found to be very thin walled with great hazard of rupture.



Figure 2. Interior extent of aneurysm just at bifurcation allowing placement of straight graft, rather than bifurcation graft.



Figure 4. Elderly patient with small aneurysm (1) and having significant generalized arteriosclerosis (2) as evident in splenic artery. Other organ disease (3) frequently found in these older patients. This patient had a circumferential external graft.



Figure 5. Mural thrombus often very thick. (1) Outer wall of aneurysm and (2) edge of lumen.

responded well to treatment during hospitalization, but one of them died several months later of intractable congestive heart failure.

TECHNICAL CONSIDERATIONS

Most surgeons qualified to perform aneurysmectomy have developed techniques based on their own experience so only a few aspects of the procedure that have been helpful in this series will be mentioned.

First of all, resection of the entire aneurysm is not necessary and will actually create undue dissection and bleeding. The aneurysm is opened after cross clamping the proximal aorta. Aqueous heparin, 3,500 - 5,000 units, is given the patient intravenously by the anesthesiologist a few minutes prior to cross clamping the aorta. The anterior wall of the aneurysm is removed, leaving the posterior wall and generous lateral walls which can later be brought up around the graft for additional support. Foley catheters, (#14 with a 5 cc bag) are placed in the proximal iliac arteries as soon as the aneurysm is opened and before the mural thrombus is disturbed. The bags are inflated to occlude the arteries so as to prevent back bleeding

and embolization of the detritus usually found in the walls of an aneurysm. The occluding balloons are more gentle to the iliac arteries than are occluding clamps. The catheters are then used periodically throughout the procedure to infuse the distal arteries with a saline solution containing heparin. This technique is illustrated in a prior publication by Bradham.¹ Anastomoses are actually made to the interior of the graft posteriorly and partially laterally, making sure that the suture gains a good purchase on the adventitia which is the only part of the wall that has any strength.

In the majority of patients, the aneurysm stops at the bifurcation and a straight graft can be anastomosed to the bifurcation (Figure 2). Significant obstruction of the iliac arteries would be an indication for a bifurcation graft but atheromata in the iliac arteries without significant obstruction is not a requisite for a bifurcation graft.

It is important that adequate tissue be interposed between the duodenum and the aortic graft. Often it is necessary to bring down the omentum between the two as the peritoneum is thin and does not always furnish an adequate buffer. This technique has been routine since the loss of the patient early in the series who developed an aortico-duodenal fistula.

The anesthesiologist is forewarned when removal of the occluding clamp is anticipated. This gives ample time to take necessary precautions to obviate any period of hypotension when the clamp is removed slowly. Postoperative renal failure has not occurred in this series.

OPERATIONS

Table I lists the operations performed. Attention is directed to *External graft* and *Wrapping of aneurysm* which are two distinctly different procedures with different long term results. External grafting has been described by Robicsek, Daugherty, and Mullen⁴ and is an excellent procedure in certain circumstances. It can be considered for the poor risk patient who has a small to medium fusiform aneurysm.

ABDOMINAL AORTIC ANEURYSMS

The procedure consists of placing the involved aortic segment in a close fitting tube of synthetic material which provides a reliable support and prevents expansion of the aneurysm. It is necessary to completely mobilize the segment of aorta so the external graft can support it circumferentially. Two patients in this series had this procedure done two and three years ago (Figure 4). Their aneurysms have not increased in size.

Wrapping an aneurysm, in the author's hands, is a procedure done only when exploration reveals circumstances mitigating against resection of the aneurysm. All four of the patients so treated in this series had extensive aneurysm formation above the renal arteries. The procedure consists of suturing a sheet of synthetic material around the aneurysm anteriorly and laterally but not posteriorly. Conceivably, it might give support to these surfaces only. Four patients had this procedure and three are dead from rupture of their aneurysms at two months, one year, and two years respectively. One patient is alive at four years. In the future, the routine use of aortography will aid in better selection of patients for operation.

RESULTS

To date, none of the patients who survived resection and replacement with a graft or an external graft have developed a pseudoaneurysm or other complication of the graft with the exception of the patient having the thrombosed graft immediately postoperative. None of the patients having a straight graft have re-

TABLE I
OPERATIONS

<i>Procedure</i>	<i>Number</i>
Resection and replacement with straight graft	28
Resection and replacement with bifurcation graft	7
Wrapping of aneurysm	4
External graft	2

Note: As mentioned in text, one patient had two graft procedures.

quired a procedure for iliac artery occlusion. Only four of the thirty-six patients who survived operation have died and all deaths were unrelated to the aneurysmectomy. One patient died of congestive heart failure, one died of a myocardial infarction, one died of carcinoma of the lung and one died of cirrhosis.

SUMMARY

Aneurysmectomy and replacement with a synthetic graft is the treatment of choice for patients having an abdominal aortic aneurysm and who have a reasonable chance for surviving the operative procedure. Although contraindications have narrowed considerably because of improved techniques and supportive care, there remains a small group of patients for whom a procedure of this magnitude is prohibitive. For those patients, having a satisfactory repair, life expectancy is much improved as the natural history of aneurysms is eventual rupture. A modest series of patients having operation for abdominal aortic aneurysm have been presented to amplify this problem.

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If aspirin fails, consider Butazolidin alka. Giving one capsule four times a day often provides prompt, pain-relieving, anti-inflammatory action to help restore joint mobility. The results you can get within a week can be maintained on as little as one or two capsules daily.

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Hollander and D. J. McCarty Jr. Philadelphia:
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Geigy

Important Note This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of fever, sore throat, oral lesions (symptoms of blood dyscrasia), dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications Children 14 years or less, senile patients, history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy, blood dyscrasias, renal, hepatic or cardiac dysfunction, hypertension, thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings Age, weight, dosage, duration of therapy, existence of concomitant diseases and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions The following should be accomplished at regular intervals. Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions This is a potent drug, its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

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CONCEPTUAL APPROACHES TO MARITAL DISCORDANCE: AN OVERVIEW FOR THE PHYSICIAN

SYLVESTER R. MLOTT, Ph.D.*
FRANK T. LIRA, M. S.*

Recent years have witnessed a steadily increasing divorce rate. From 1963 to 1973 the rate of divorce nearly doubled, increasing from 2.3 to 4.4 per 1,000 population.¹ This statistic does not account for the many discordant marriages which lack even the mutuality required to effect a resolution.

In his daily practice, the physician is perhaps the professional most exposed to marital disharmony. He often finds himself in the difficult position of being regarded as respected ally and confidant by patients who are experiencing severe marital difficulties and contemplating divorce. While he may be reluctant to become involved, he is nevertheless called upon to share his respected opinion, to offer advice, or to prescribe that magical solution which will alleviate the suffering of the patient whose marriage is obviously floundering. When this situation arises, the physician must decide whether to deal with the problem himself or refer the patient to another helping professional. The aim of this paper is to extract and organize information which the physician may apply to this problem area.

Explanations regarding causal factors leading to divorce generally represent three approaches: the demographic, the interpersonal-dynamic, and the societal-theoretical.

DEMOGRAPHIC APPROACH

First, perhaps the most popular explanations are generated by demographic data which attempt to correlate rate of application for divorce with such demo-

graphic factors as sex, age, education, occupation and income. Such demographic data reveal that for males, the most prevalent age range for divorce is 45 to 54, after which there is a steady decline. The same age range applies to women, but the frequency in this age group for females is double that of males.

Education level presents another factor to be considered in divorce. For males, the highest percentage of divorces are initiated by individuals with the lowest level of education. For females, the reverse is true, with the highest percentage of divorces being initiated by females with the highest level of education.²

Statistics examining the occupation factor show that male domestic servants file for divorce more frequently than members of any other occupational field, including managers, administrators, salesmen, technicians and other professional workers. Farmers and farm laborers demonstrate a very low rate of divorce for males and females. Females in administrative and managerial positions show the highest.²

A third factor is the relationship between income and divorce. For males, the highest rate of divorce is associated with the lowest levels of income. For the females, the highest rate of divorces sought is associated with the highest levels of income.³

While these investigations delineate factors obviously associated with divorce patterns, they cannot establish cause and effect relationships between divorce and those variables previously discussed. Nevertheless, these findings strongly support the inclusion of such demographic factors in any consideration of divorce.

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INTERPERSONAL-DYNAMICS APPROACH

Interpersonal - dynamics explanations provide a more theoretical approach to understanding marital disharmony. Dr. Lawrence Kubie⁴ offers one such explanation which rests on the theory that each marital partner places conscious and unconscious demands on his mate as well as his marriage. He suggests that choosing a mate is one of the most confusing steps a person takes in life. He theorizes that although people choose mates whose interests and habits are incompatible with their own, this is not the primary cause of confusion. Rather, it is caused by the fact that each marriage partner is unaware of those unconscious purposes which determine his choice. Kubie observes that marriage in our culture is based on the concept of romantic love, which has survived through centuries of cultural evolution. Closely related to the romantic ideal is the belief that a principal function of marriage is to increase one's personal happiness. Steadily soaring divorce rates suggest that neither of these factors presents an effective predictor of harmonious marriage.

Albert Ellis⁶ believes most couples who seek marital counseling are victims of neurotic interactions in marriage. Ben J. Ard⁵ suggests that these interactions occur between marital partners who are theoretically capable of engaging in satisfactory dyadic interactions but who actually engage in irrational self-defeating behaviors. These neurotic interactions evolve from unrealistic and irrational ideas that comprise belief systems on the part of one or both partners. Irrational beliefs which lead to neurotic interactions include the following: (1) It is necessary for an adult to be approved or loved by all significant people he encounters; (2) An adult should or must be perfectly confident, adequate and intelligent; (3) A person should severely blame himself for mistakes in order to avoid similar mistakes in the future; (4) Unhappiness is generally caused by external forces which

one is powerless to control; and (5) The opinions of others are more important than one's opinion of himself.

The communications approach to explaining and resolving marital difficulties has gained increased support and application during recent years. Communication is the primary requirement for the development and maintenance of interpersonal relationships. Communications is associated with creating as well as solving problems in the family. Ideally, communications in marriage represents the efforts of marital partners to establish a commonality regarding some area of experience. Regardless of whether the partner is attempting to share ideas, meanings or feelings, his attempts are constantly directed toward creating an image in the mind of the receiver. No doubt many marriages flounder on this rock of non-communication. Marriages apparently vary considerably, both in the degree to which partners communicate with each other and in the areas in which communication occurs.⁷

When marital partners are together it is impossible for them not to communicate. Communication occurs along verbal and nonverbal modes. The raising of an eyebrow, a frown, the bringing of flowers, a handshake, a surly grumble, an unexpected touch of the hand, a kiss, a barely audible sigh—these are all examples of nonverbal communicative behavior that direct some message to the other person.⁸ Verbal communications are often clearer but may bear such subtle components as fluctuations in vocal tone, pitch or tempo. The effectiveness of the communication is determined by the extent to which the message received by one partner corresponds to the message intended or the feeling experienced by the sender. Kahn⁹ suggests a major aspect of marital disharmony is the misunderstanding of intentions that are communicated nonverbally. Since nonverbal communication is often subtle, there is a greater risk of misinterpretation. Clarification of non-

APPROACHES TO MARITAL DISCORDANCE

verbal messages must generally occur on a verbal level. Such a message may be regarded as non-significant or not really present, so clarification is seldom requested or provided. Kahn emphasizes that the accuracy of these nonverbal communications is closely related to marital satisfaction. Lederer and Jackson¹⁰ relate marital trust to communication. When spouses, by their behaviors, are communicating clearly with each other, there is trust because they read each other clearly. Each partner can understand and accept the significance, the intent, the values and the meanings of the other's communicative behavioral repertoire. If there is doubt, each freely requests clarification.

Clements¹¹ in his research, found a related variable associated with marital stability, namely, an awareness of the effects of one's own behavior on one's spouse and the willingness to modify those behaviors. The fact that all behavior has some communicative components, verbal or nonverbal, makes this variable particularly important in the communication model. Jones¹² seems to draw the same conclusion when he suggests that one's maturity or growth can be assessed by the effectiveness and intimacy of his communications with significant others in his life.

Another aspect of the interpersonal-dynamic approach to explaining divorce is sexuality, which includes sexual compatibility and adjustment. Johnson and Masters¹³ suggest that the incompatible male partner is plagued by three major types of impotence: (1) failure to achieve erection; (2) inadequate erection; and (3) non-emission erection. These researchers stress the importance of the marital interaction as well as previous interactions, suggesting that data collection in the context of marital counseling should include the male's attitude toward his marital partner; earlier sexual interactions with prostitutes who insisted on rapid performance; whether waning sexual performance is temporarily associated

with marital disharmony; and whether there is an active homosexual history.

Female sexual incompatibility or psychosexual inadequacy can be understood by collecting information in the areas of (1) attitudes toward sex and its significance within the marriage; (2) degree of regard for the marital partner; and (3) fear of pregnancy. Surveys have shown that the two basic deterrents to female sexual responsiveness are fatigue and preoccupation.

SOCIETAL-THEORETICAL APPROACH

A third approach to understanding divorce views marital disharmony as a function of the culture in which it occurs. The societal-theoretical approach relies on sociological data to generate hypotheses regarding divorce. This approach is represented by Alvin Toffler¹⁴ who has observed the phenomenon he terms the serial marriage—a pattern of successive temporary marriages which are consistent with today's transient society. Toffler relies on the theories of numerous social theorists including Jessie Bernard when he concludes that the transient marriage is the inevitable outgrowth of a society whose members rent their automobiles, trade in their dolls instead of mending them, and discard clothing after a single wearing. Toffler does not appear to be speculating when he suggests that in the near future one's marital status will be regarded as a trajectory which provides for a series of marriages, each representing an extended developmental stage. While such predictions seem farfetched, the fact is that one in four of today's bridegrooms will make at least another trip to the altar in his lifetime.

While this presentation does not include an exhaustive account of all information which might be brought to bear in the understanding of divorce, it should provide the physician some perspective in his approach to the problem. The demographic, interpersonal-dynamic, and societal-theoretical approaches have

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been assigned their classifications with the intention of organizing the mass of information that has addressed the problem of divorce. It is suggested that information from each of these areas be considered in the physician's approach. At this point, a brief guideline is provided to assist the intervening professional in dealing with the couple who confront him with their failing marriage.

First, the physician should help them bring into focus how each partner is contributing to the situation, keeping in mind that there is no such thing as an innocent victim of interpersonal difficulties.

Secondly, the area of problems in intimacy should be explored since this is one of the most disturbing interpersonal difficulties couples encounter. People who live together on the most intimate terms suffer most from the rough spots in their mates. For instance, with the highest divorce rate occurring during the menopausal period, loss of reproductive function may have psychological concomitants which preclude satisfactory sexual participation or open interpersonal communication. If this is the problem, it should be brought into the open and discussed.

A third area where most marital difficulties may occur and flourish is in situations where gratification of personal need becomes more important than concern for the welfare of the other.¹⁵ A number of theorists believe that a satisfactory marriage rests on the successful reciprocal gratification of needs.¹⁶ The physician must not impose his own moral standards but should encourage understanding or at least exploration of the personal needs of each partner. The solution lies in the recognition, analysis, and understanding of the personal need which interferes with the needs and interests of both partners and encourages a mutually trusting and sharing relationship. It is generally recognized that reciprocal gratification leads to mutual marital satisfaction.¹⁷

Another area for the physician to probe is whether any earlier traumatic experi-

ence is responsible for the current marital difficulties. Repressed memories can influence present behavior and it must be remembered that repression can occur in people who, for the most part, are psychologically healthy and sound.

One cause of marital conflict is often due to feelings of being "taken for granted" by the other partner. Here the physician can be of value in helping the couple explore their individual needs for attention, praise and encouragement from each other.

It is probable that many marriages flounder due to non-communication. For instance, many husbands may feel confident that they are communicating successfully their love for their wives through the sexual attention he pays her and for the daily living necessities which he provides for her and the family. As he perceives his behavior, he is saying, "I love you." Does the wife decode this message, or does she, due to the influence of such factors as Hollywood and the many women's magazines believe "I love you" can only be decoded in terms of small gestures, gifts, or indications of attention ordinarily associated with courtship? Perhaps here the physician can help the male spouse recognize what may seem trivial in the masculine world is vital to the female and that perhaps he can listen more accurately to his wife, which may result in a more harmonious relationship.

The above listed aids for the physician are not meant to be all-inclusive by any means but serve merely as an introduction to guide the physician in helping his patients understand their marital conflicts.

Therapy actually preserves many marriages. Therapeutic changes occur not only in the individual undergoing therapy, but also in his or her mate, since an alteration in one member of a family is likely to affect the behavior of people with whom he is in close contact.¹⁸ Although therapy may involve interaction with a psychiatrist, psychologist, social worker or marriage counselor, the most effective

APPROACHES TO MARITAL DISCORDANCE

therapy may occur with the family physician who listens and cares.

SUMMARY

Studies applied to the understanding of marital discordance were conceptualized as representing three general approaches. Demographic approaches include correlational studies which match such factors as sex, age, income, educational level and vocation. Interpersonal-dynamics explanations attempt to isolate and describe those factors existing between married individuals which inhibit

or enhance mutual satisfaction. Societal-theoretical approaches observe marital disharmony in the context of the culture in which it occurs.

The general practitioner is seen as the helping professional who is most likely to be confronted with the failing marriage of his patients. Without moralizing, the physician can be instrumental in preserving a salvageable marriage through active though possibly brief counseling in his daily practice.

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President's Pages



Dear Fellow Physicians:

As reported in the last issue of the Journal, a Training Conference and Speaker's Seminar was held in Charleston at the Mills Hyatt House on August 15, 16, and 17th with twenty-one participating physicians attending at their own expense. This was an intensive session, lasting all day Saturday and until noon on Sunday. All of us in attendance felt that it was really worthwhile and would improve and enhance our ability to represent ourselves and the medical profession. We are hopeful that these Seminars can be held yearly, and that more and more of our physicians will take time and become involved in these Training sessions.

The medical liability insurance continues to be in the forefront of our activities. The Liability Committee has had a second meeting and on September 11, at 4:00 P.M., a meeting was held at the Summit Club with the Liability Committee, Public Relations Committee, and the Legislative Committee in attendance. There were representatives of twelve other professional groups present, and these visitors all participated in a lively discussion and exchange of opinion and ideas. Dr. Kilgore, as Chairman of the Liability Committee, presented items under discussion for the Liability Committee, and there were many interesting comments coming from the lawyers involved, such as the Trial Lawyers and the South Carolina Bar, Hospital Association, Dental Association, Nurses, Accountants, etc. This session lasted for 2½ hours and was followed by a supper for those able to remain. It was our opinion that this first step will do much to focus the attention of all professions in South Carolina that the medical liability problem is only the first step before all of the other professions will be involved with their liability insurance. It was stressed to those in attendance that this was a problem involving everyone, and that the solutions had to be obtained by having an input of all ideas and opinions so that legislation could be proposed and enacted that will gain wide enough support to be successful. It was emphasized that only by an aroused public opinion demanding that solutions be sought, and legislation passed, will the legislators enact meaningful legislation.

Everyone in attendance at this meeting was urged to go back home and to talk to the public and to the legislators and impress upon them the urgency of this crisis situation that is still with us, emphasizing that the JUA is only a temporary stopgap that will run out December 31, 1977. Meaningful reform legislation has to be passed in the 1976 session of the legislature so that the private insurance industry can come back into the professional liability field in South Carolina and operate on a competitive basis.

EVERY PHYSICIAN IN SOUTH CAROLINA SHOULD JOIN THE TEAM TO GET THIS MESSAGE ACROSS NOW!

The first meeting of the South Carolina Medical Injury Insurance Reparation and Advisory Committee, known as MIIRA, was held at 2:00 P.M. on September 11, 1975, and Don Kilgore and I attended as members of that Committee. This Committee was divided into three sub-committees: Legal, which has Dr. Kilgore as a member; Medical, which has me as a member; and insurance. Each has been assigned various subjects for study. Committee meetings will be held in two weeks, and a further meeting of the entire Committee will be held in one month. It is our objective to work with this Committee as

expeditiously as possible so that meaningful proposed legislation can come early in 1976, to be presented to the South Carolina House and Senate.

The Executive Committee of Council will meet on September 18.

On October 16, 17, and 18, the entire Council will hold a weekend retreat and meeting at Hilton Head, South Carolina. This will be a brainstorming type session to discuss all of the activities and goals of the Association, and attempt to acquaint each and every member of Council with the myriad of problems and opportunities and challenges that we face today.

The 1975 S.C.M.A. SOCPAC Mid-Winter Conference will be held on November 14, 15, and 16, 1975, at the Sheraton Motor Inn, Greenville, South Carolina. All standing committees of the South Carolina Medical Association are asked to meet and bring reports to this Conference, to be referred to the Reference Committees for the purview of the House of Delegates. All Delegates, Committee members, and other interested members of the South Carolina Medical Association are invited and urged to attend your Mid-Winter meeting.

The Executive Committee will decide at its September 18th meeting if it is necessary to call a special session of the House of Delegates, as suggested in my last letter to you. This action will be publicized as soon as a decision is made.

WORKING TOGETHER WORKS!

PARTICIPATE AND CONTRIBUTE IN THE DISCUSSION OF THE MANY PROBLEMS AND OPPORTUNITIES FACING MEDICINE TODAY, BOTH AT YOUR LOCAL HOSPITAL STAFF LEVEL, MEDICAL SOCIETY LEVEL, STATE LEVEL, AND AMA LEVEL! A WORKING, UNITED, COHESIVE EFFORT WILL CAUSE THINGS TO HAPPEN AND FURTHER THE PROGRESS OF ORGANIZED MEDICINE SO THAT WE MAY CONTINUE TO PROVIDE QUALITY MEDICAL CARE, WITH A FREE CHOICE OF PHYSICIAN, FOR THE CITIZENS OF SOUTH CAROLINA.

Sincerely yours,
C. Tucker Weston, M. D.
President
South Carolina Medical Association



50 YEARS AGO

September 1925

By joint effort of Beaufort, Georgetown, and Marion Counties, the State, and the International Health Board a program was made for the control of malaria. There was a discussion of the good work of the South Carolina Tuberculosis Association and an outline of its program.

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When a telephone prescription for pain relief is necessary or convenient, you can call in your order for Empirin Compound with Codeine in 45 of the 50 states† That includes No. 4, which provides a full grain of codeine for more intense, acute pain.

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Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

Overdosage may cause a curare-like action, with loss of voluntary muscle control.

For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and this possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evidenced by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

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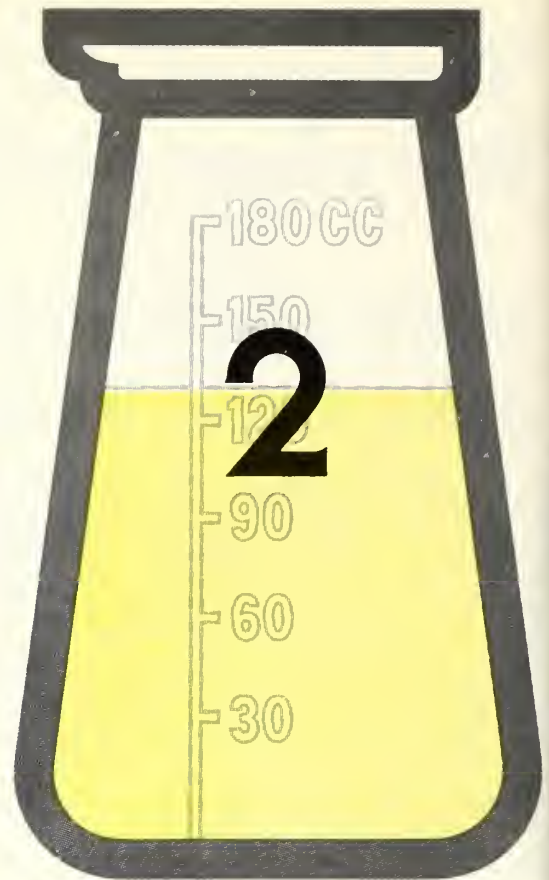
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cystitis

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic non-obstructed urinary tract infections (primarily pyelonephritis, pyelitis, and cystitis) due to susceptible organisms. **Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials, including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

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Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

* WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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Hydrochlorothiazide to help keep
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Editorials

Stress—General or Specific?

During his student days in pre-World War I Vienna, Hans Selye noted that many of the patients presented in lectures and classes had characteristics in common. The professors were interested only in the peculiar symptoms of each disease which separated it into a class of its own and completely disregarded the universal symptoms. Hans Selye questioned his professors about the universal symptoms of disease but was rebuffed and advised that only the distinguishing findings were important.

The young student forgot all about this early experience until several decades later, after achieving considerable success in laboratory investigating and settling in Montreal. Deeply involved in an experiment with carcinogenic agents in mice, he suddenly noted that both the controls and the experimental animals in long term experiments exhibited common symptoms of debilitation. He then recalled his Vienna observations and went on to develop his theory of The General Adaption Syndrome with stages of shock, counter-shock, and fatigue. The patients in Vienna, with various diseases all showed in common, symptoms of lassitude, fatigue and debilitation. The rats in Montreal, those given doses of carcinogenic agents and those given control agents over several months, all developed symptoms of lassitude, fatigue, and debilitation. Selye had recognized the General Adaption Syndrome.

This is, as named, a general syndrome in response to stress. The response is the same regardless of the stress encountered.

This general response to stress has long been recognized and accepted. However, recently, theorists are questioning that perhaps there is a specific response to stress, differing with the stress agent or perhaps differing with the stressed organism. Irvin and O'Sheal's article on Stress and Myocardial Infarction throws some additional light on this perplexing problem.

EEK

Standards

Clifton Fadiman was an idol of my childhood. This intellectual's intellectual was host of a radio word game that brightened my Sunday afternoons, was an editor of "The New Yorker," and was Editor-in-Chief of the Book-of-the-Month Club, which was at the time about the far limit of my literary vision. Yesterday I heard him, again on radio, decrying the erosion of precision in our language. As an example of his lamentations, he recalled that this teenage daughter recently returned from the hair dressers reporting that she had been exhorted to "naturalize" her hair. By "naturalization" it turned out that the hair dresser meant dying the hair—exactly the antithesis of the real meaning of the word.

Fadiman's experience hit a sympathetic chord with me. It seems that this lack of precision in our language often is the direct desire of communicators to obfuscate, cloud, and misdirect the impact of their message. Frequently government and professional communicators are at the bottom of this clouding.

For example: A recent communication

from the Department of Health, Education, and Welfare to a South Carolina school district with which I am intimately familiar referred to "the 62% minority in your schools." A 62% minority? Pretty close to a majority I would say.

An editorial in *The State* on July 4, 1975, discussed displaying "private parts of the human body" on movie screens. Specifically, it discussed the displaying of "private parts" on a 35 by 70 foot screen, 54 feet above ground in Jacksonville, Florida. Obviously the parts of the body displayed on this screen were not private to the individual displaying them, nor to the thousands viewing them.

The title of *The State* editorial was "Court Twists Logic." Let us all try not to twist language to make it convey a message that is not there. As Clifton Fadiman said: "What can be in store for a nation that lets its language be treated like that?"

EEK

No Double Standards

Speaking of *The State* newspaper, a front page, bold type statement, signed by Ambrose Hampton, Publisher, appeared in the July 10 issue proclaiming that the State-Record Company papers would no longer accept legal advertising at an old, long-established, and now obsolete price rate. He stressed that after his deadline, unless submitted at the new rate, legal notices would not appear in the paper.

Now I completely understand, endorse, support, and respect this decision by the newspapers' management on the operation of the paper and their right to refuse to operate at a loss. Legal advertising is almost as necessary to the welfare of South Carolina as medical care. I hope the newspapers will resist the double standard and will resist criticizing physicians too harshly when we attempt to claim just recompense from governmental agencies for our best efforts.

EEK

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124th ANNUAL CONVENTION OF THE AMA

JUNE, 1975

JOHN C. HAWK, JR., M.D., DELEGATE

AMA conventions are remembered for various features—or maybe forgotten for lack of any distinctive decision or event. Just as “beauty is in the eye of the beholder,” so, different persons will view the 124th Convention of the AMA in quite different lights. By the time this report is published in the Journal, all SCMA members will have had the opportunity to read various news accounts of convention activities and of actions taken by the House of Delegates, so I will not attempt a detailed listing of these. However, a few comments from a South Carolina perspective may be of interest.

To some, this AMA convention will be remembered primarily as the last one ever held at Atlantic City. Others will recall it as the smallest convention, from the standpoint of general attendance, in recent memory. Only 5,202 physicians were registered, as compared to 24,268 at the Annual Convention ten years ago. Total registration, including non-physicians, was 12,957. The site and the sparse attendance are closely related. I heard no regrets about the decision (previously made) never to return again; instead, only disparaging comments about ever coming at all. Atlantic City is trying to “come back” as a convention city as well as a vacation resort, but the effort has been a dismal failure thus far.

Still others will note that this convention—especially the meeting of the House of Delegates—was a quiet one. We had no picketing, no demonstrations, no visit by the President or Vice-President of the United States, no need for extra security measures, no single issues for heated debate—like Medicare or PSRO.

IMPORTANT POSITIVE ACTIONS

Nevertheless, I believe that this 124th Annual Meeting of the House of Delegates may well go down in history as a turning point for the AMA, leading to a stronger, more vigorous and effective Association. I base this optimistic appraisal on the following actions:

1. The House faced squarely the issue of fiscal responsibility—the need for a financially stable organization—and voted a Dues Increase for regular members from \$110.00 to \$250.00 per year. Dues for Interns and Residents were raised to \$35.00, and dues for Medical Students were kept at \$15.00. This action came despite warnings from several delegations, notably that of New York, that the dues increase might result in many membership withdrawals, estimated as high as 15,000 nationwide. Your South Carolina Delegation believes this dues increase is essential, and urges all physicians

in the State to join the AMA and also to pay the special assessment of \$60.00 set last winter. This is not to say that we are in complete agreement with all the actions and positions of the AMA—far from it, as I will mention later in this report. But the AMA is the one organization of physicians with a sufficiently broad base to represent the medical profession in dealing with governmental agencies. We need for the membership to be even larger, particularly among the practicing physicians of the nation.

In support of recommended economy measures, the House voted to discontinue publication of PRISM as soon as practicable under present commitments, and to place distribution of TODAY'S HEALTH on a subscription basis, rather than blanket distribution to all AMA members as a membership benefit, as it has been in the past. A motion to discontinue publication of TODAY'S HEALTH entirely was defeated by the House.

The House also approved structural changes at AMA headquarters designed to reduce operational costs.

2. The House of Delegates gave resounding support to the Board of Trustees for instituting a suit against the Federal Government (HEW), which had already resulted in an injunction by Judge Julius Hoffman to halt application of Utilization Review regulations protested by the AMA. Most delegates considered the cost of this suit to be money well spent. The House also supported the Board in its decision to go to court, if necessary, to block putting into effect the so-called MAC program, which would limit physicians in the drugs they could prescribe for their patients under government financed programs.

As a matter of fact, these actions by the Board were largely responsible for the change in attitude of the House toward the Board. At Portland six months ago (Clinical Convention, 1974), the House had been highly suspicious of Board actions and openly rebellious toward the requested dues increase, and toward some of the economy measures recommended by the Board. At Atlantic City, however, the House gave warm approval to most of the actions taken by the Board during the intervening six months.

3. The House approved the Board's recommendation to establish an AMA reinsurance facility to support and back up the efforts of state medical societies in setting up “captive”

medical liability insurance companies. According to the feasibility report of the Board, \$20,000 will be needed just to begin filing for incorporation, a minimum of \$1.5 million will be needed in reserve, and at least five states will have to participate, with a minimum of \$12 million provided in annual premiums. Since a state would need 3000 to 5000 participating physicians in order to enroll, smaller states like South Carolina would have to group together with a neighboring state or states to attain the required number.

The AMA has already provided much useful information and assistance to states in the current "malpractice" insurance crisis, including the recommendation of model legislation to be proposed to state legislatures. This has been utilized extensively by the SCMA in proposals to the South Carolina legislature, including the setting up of the Joint Underwriting Association (JUA).

4. The House finally approved, after vigorous debate and many revisions, a statement relating to the use of strikes by physicians as a means of protest. The word "strike" did not appear in the final statement, and even the title was changed, but there was no doubt of the implications involved. It is of sufficient importance to quote in its entirety:

A Statement of the Physician's Commitments to Patients and the Physician's Practice Rights

Resolved, That the primary commitment of the American Medical Association and its physician members is to the essential medical needs of the people of this nation; and be it further

Resolved, That the American Medical Association recognizes that it is the inalienable right of physicians to decide for themselves the circumstances under which they can or cannot continue to practice their profession; and be it further

Resolved, That the American Medical Association recognizes that physicians are entitled to use all available legal means, without jeopardizing the medical care of their patients, to protest when intolerable and unwarranted burdens are placed upon their patients, the Association or its members; and be it further

Resolved, That the American Medical Association continue to study the effects of changing socioeconomic conditions on the ability of physicians to practice medicine.

5. The House vigorously opposed P.L. 93-641, the Health Resources and Planning Act of 1974, and strongly supported the Board of Trustees in any action, including legal action, which may be deemed appropriate and effective in preventing the implementation of P.L. 93-641.

These were the actions, as I see them, which most clearly demonstrated the determination of the House to strengthen the AMA and make it a

Rondomycin (methacycline HCl)

CONTRAINDICATIONS Hypersensitivity to any of the tetracyclines.

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**

Usage in pregnancy. (See above **WARNINGS** about use during tooth development.) Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fetal bone growth rate observed in premature given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients must be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes, exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.

Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.

USUAL DOSAGE: Adults—600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea: In uncomplicated gonorrhea, when penicillin is contraindicated, "Rondomycin" (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule: 900 mg initially, followed by 300 mg q i d for a total of 5.4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of "Rondomycin" (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.

Eaton Agent pneumonia: 900 mg daily for six days.

Children—3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.

Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.

In streptococcal infections, a therapeutic dose should be given for at least 10 days.

SUPPLIED: "Rondomycin" (methacycline HCl): 150 mg and 300 mg capsules; syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev. 6/73



WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512



**When the focus is on bronchitis due to
susceptible strains of *H. influenzae* and pneumococci***

Rondomycin[®] 300 mg. **[methacycline HCl]** Capsules

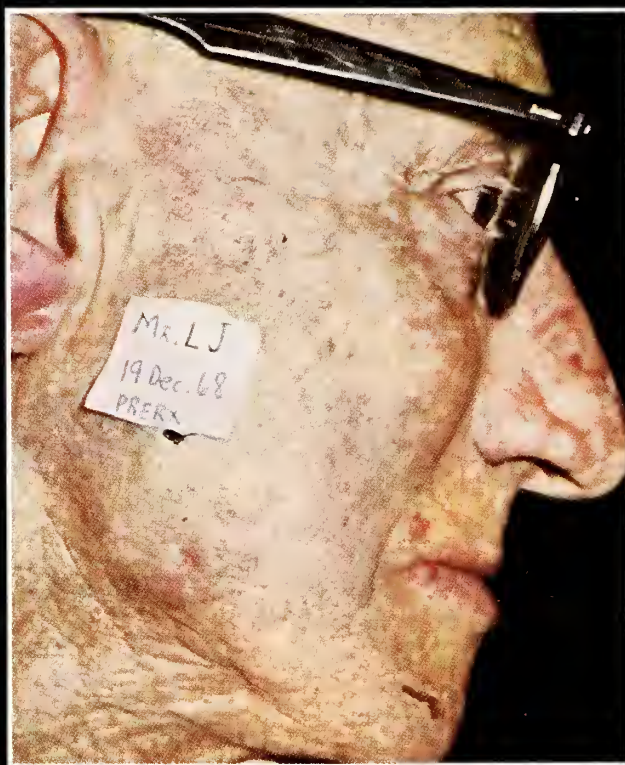
Delivers from the very first dose:

**Studies show that after the first dose serum levels rapidly rise above
minimum *in vitro* inhibitory concentrations**

*Since many strains are known to be resistant, routine sensitivity testing is recommended

the sun and solar keratosis...

Overexposed



and often underdiagnosed

Solar keratosis is not an uncommon medical problem.

Of course, the prevalence of keratotic lesions is greater in locations south of the 38th parallel—the so-called "Solar Keratosis Belt"—receiving the greatest amounts of solar radiation. However, solar keratosis can occur among any light-skinned population, usually in persons over 40, wherever people are subject to extended exposure to the sun.

Solar keratoses are generally not difficult to identify.

These skin lesions are usually multiple, flat or slightly elevated, brownish or red in color, papular, dry, rough, adherent and sharply defined. They are found on areas of the skin having extensive exposure to sunlight. Clinical characteristics of the lesions, their predominant location on exposed surfaces, the age of the patient and his skin type are important considerations in the diagnosis.

Solar keratoses can, and should, be treated because they are potentially premalignant.

Chronic exposure to sunlight frequently leads to degenerative changes in the skin. This can often result in the development of multiple, potentially premalignant keratotic lesions. Therefore, early detection and treatment is advisable.

Treatment with Efudex (fluorouracil) provides a high degree of effectiveness with a low recurrence rate, ease and convenience of therapy, low incidence of scarring, excellent cosmetic results in most cases, and a high level of patient acceptability.

Efudex® 5% Cream

fluorouracil/ Roche®

Because there may be more than meets the eye.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to

respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dis-

pensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris (hydroxymethyl) aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

viable "umbrella" organization, which hopefully will merit continued and increasing support by the physicians of this country.

ON THE MINUS SIDE

On a few other issues, the action of the House, in my opinion, will have to be considered "on the minus side"—weak, or misguided, or even downright wrong; these included:

PSRO Policy: The House was obviously unwilling to enter into long debate about PSRO, and defeated a Resolution calling for repeal of the PSRO law. Instead, the PSRO policy that the AMA adopted at the 1974 Annual Convention was reaffirmed. Basically, this called for AMA action to seek constructive amendments to the law and appropriate regulations and directives. This is not the policy for which your delegation has worked diligently in the past. We have favored forthright action to seek repeal. We continue to question the effectiveness of the proposed "monitoring" of the PSRO program. However, in House discussion, it was again emphasized that if the PSRO program becomes too restrictive, the Board has the authority to seek repeal. The possibility of legal action was also cited again. But it must be pointed out that just recently, under a grant of nearly a million dollars from the HEW, the AMA has published a nearly three inch thick volume containing 815 pages, weighing 4½ pounds, entitled "Model Screening Criteria to Assist Professional Standards Review Organizations." It appears unlikely, therefore, that the AMA involvement in PSRO's will be changed.

Review Standards for Federal Hospitals: Three resolutions addressed themselves to varying aspects of the subject of utilization review and peer review of programs in VA and other federally controlled hospitals. Many physicians, including the members of your delegation, have felt strongly that any such procedures proposed for civilian hospitals, should certainly be applied with equal vigor (and actually should have been tried first) in federal hospitals. In lieu of the three new resolutions, the House, accepting the advice of the Reference Committee, simply reaffirmed Resolution 107 of the 1974 Annual Convention which reads as follows:

"Resolved, That this House of Delegates reaffirm its belief that Peer Review of medical health care delivery in federal institutions is needed and desirable, and that such government hospitals and medical facilities should continue to be reviewed by the Joint Commission on Accreditation of Hospitals or similar medical associations review bodies in the same manner and by the same standards as those used for private community hospitals."

PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. Usage in Pregnancy: Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. Children and Adults: Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies.* Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

ROERIG *Pfizer*

A division of Pfizer Pharmaceuticals
New York, New York 10017

NSN 6505-00-148-6967

**Pinworms, roundworms controlled
with a single, non-staining dose of
ANTIMINTH[®]
(pyrantel pamoate)**

equivalent to 50 mg pyrantel/ml.

ORAL SUSPENSION

Since there continues to be serious question as to the effectiveness of review procedures in federal hospitals at present, many of us felt that a much stronger statement should have been adopted.

INAUGURAL ADDRESS OF PRESIDENT

Dr. Max Parrott of Oregon, in his inaugural address as President of the AMA, stressed that maintaining the high quality of medical care is the overriding goal of the AMA. He described the national debate on health and medical issues as a clash between governmental utilitarianism and the humanism of the medical profession. He decried the fact that "health care planners and regulators see medical care as little more than a numbers game—if only the commodities of health care can be more efficiently organized, assembly-line style, if only the providers of care can be better coordinated as a work force, then the consuming public will be eternally blessed." He noted that such government programs as PSRO's and HMO's were designed to produce efficiency in delivering a "commodity." He warned, however: "medically speaking, efficiency means something far different from quality—and a pre-occupation with it could subvert quality."

"Efficiency means organization for optimum production at the least cost in time and money. Quality in medical care means giving the best appropriate service—regardless of the time required—and regardless of cost."

Dr. Parrott's surprising suggestion that sweeping changes be made in the top level organization of the AMA, including abolishing the offices of AMA vice-president, president, president-elect, and immediate past president, was referred to the AMA Council on Long-Range Planning and Development for report at the interim meeting in Honolulu.

Many will recall that Dr. Parrott has visited South Carolina several times, including the SCMA Annual Convention in 1972.

ELECTIONS

Dr. Richard Palmer, of Alexandria, Virginia, was named President-Elect by a comfortable 157-88 margin over Dr. William Sodeman. Dr.

Palmer has been Chairman of the Board of Trustees during the past year, and took part in our Annual SCMA Convention last May.

Dr. George W. Slagle, of Battle Creek, Michigan was elected AMA Vice-President.

New members of the Board of Trustees are Dr. Joseph H. Boyle of Los Angeles, California, and Dr. Lowell Steen of Hammond, Indiana. Dr. Jere W. Annis of Florida, Dr. Joe T. Nelson of Texas, and Dr. Robert B. Hunter of Washington were reelected to the Board of Trustees.

At the Board re-organization meeting, held immediately after the House adjourned, Dr. Raymond T. Holden of Washington, D. C., was named Chairman of the Board, Dr. Annis, Vice-Chairman, and Dr. John H. Budd of Ohio, Secretary-Treasurer of the AMA and Secretary of the Board. The Board's Executive Committee will consist of Drs. Parrott, Palmer, Holden and Annis, plus immediate Past President Malcolm C. Todd of Long Beach, California, and Trustee Frank J. Jirka, Jr. of Berwyn, Illinois.

SCMA MEMBERS ATTENDING

Attending as representatives of the SCMA were John C. Hawk, Jr., and Harrison Peeples, delegates; Tucker Weston, alternate delegate; Charles Johnson, executive director; and J. D. Gilland, president-elect. Dr. William Perry, our other alternate delegate, was unable to attend. We were sorry that none of our wives chose to attend with us, but their enthusiasm for the convention site was even less than our own.

We were pleased to have Auxiliary representatives join us for some of the social events; Sara Shingler, Auxiliary President, and her husband Jack; Billie Brady, immediate Past President, and her husband Wayne; and Sheila Davis, Auxiliary delegate.

1975 CLINICAL CONVENTION

The 1975 Clinical Convention will be held in Honolulu, Hawaii, November 28 through December 6, 1975. The locale should engender a good deal of interest and enthusiasm. We hope there will be a good representation of SCMA members. We will have a hospitality room at the Headquarters Hotel. Please join us whenever you can.



Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

Found useful in the management of vertigo* associated with diseases affecting the vestibular system.

Can relieve nausea and vomiting often associated with vertigo.*

Usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.

Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.

Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for use, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.


Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG 
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert[®]/25 (meclizine HCl) 25 mg. Tablets for vertigo*

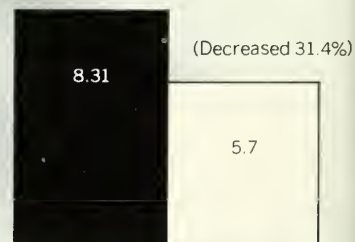


Would sleep with fewer nighttime awakenings benefit your patients with insomnia?

Highly predictable results for your patients with trouble staying asleep...

...can be obtained with Dalmane (flurazepam HCl). As shown below, Dalmane significantly reduces nighttime awakenings.¹⁻⁴

Average Number of Nighttime Awakenings¹⁻⁴
(Four Geographically Separated Sleep Research Laboratory Clinical Studies, 16 Subjects)



3 placebo
baseline
nights

7 Dalmane
(flurazepam HCl)
30 mg nights

And for those with trouble
ling asleep or sleeping
ng enough...

... Dalmane (flurazepam HCl)
o delivers excellent results.
nically proven in sleep research
poratory studies: on average,
ep within 17 minutes that lasts
o 8 hours.⁵

Dalmane (flurazepam HCl)
relatively safe, seldom
uses morning "hang-over".

...and is well tolerated. The
ual adult dosage is 30 mg *h.s.*,
t with elderly and debilitated
tients, limit the initial dose to
mg to preclude oversedation,
ziness or ataxia. Evaluation of
ssible risks is advised before
escribing.

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Vogel GW: Data on file, Medical Depart-
nt, Hoffmann-La Roche Inc., Nutley NJ
Dement WC: Data on file, Medical Depart-
nt, Hoffmann-La Roche Inc., Nutley NJ
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ffmann-La Roche Inc., Nutley NJ

ore prescribing Dalmane (flurazepam
HCl), please consult complete product
ormation, a summary of which follows:

Indications: Effective in all types of insomnia
characterized by difficulty in falling asleep,
quent nocturnal awakenings and/or early
orning awakening; in patients with recurring
omnia or poor sleeping habits; and in
ute or chronic medical situations requiring
stful sleep. Since insomnia is often transient
d intermittent, prolonged administration is
enerally not necessary or recommended.

Contraindications: Known hypersensitivity
flurazepam HCl.

Warnings: Caution patients about possible
combined effects with alcohol and other
CNS depressants. Caution against hazardous
occupations requiring complete mental alert-
ness (*e.g.*, operating machinery, driving).
Use in women who are or may become preg-
nant only when potential benefits have been
weighed against possible hazards. Not
recommended for use in persons under 15
years of age. Though physical and psycho-
logical dependence have not been reported
on recommended doses, use caution in
administering to addiction-prone individuals
or those who might increase dosage.

Precautions: In elderly and debilitated, initial
dosage should be limited to 15 mg to preclude
oversedation, dizziness and/or ataxia. If
combined with other drugs having hypnotic
or CNS-depressant effects, consider potential
additive effects. Employ usual precautions
in patients who are severely depressed, or
with latent depression or suicidal tendencies.
Periodic blood counts and liver and kidney
function tests are advised during repeated
therapy. Observe usual precautions in
presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness,
lightheadedness, staggering, ataxia and
falling have occurred, particularly in elderly

or debilitated patients. Severe sedation,
lethargy, disorientation and coma, probably
indicative of drug intolerance or overdosage,
have been reported. Also reported were
headache, heartburn, upset stomach, nausea,
vomiting, diarrhea, constipation, GI pain,
nervousness, talkativeness, apprehension,
irritability, weakness, palpitations, chest
pains, body and joint pains and GU com-
plaints. There have also been rare occurrences
of sweating, flushes, difficulty in focusing,
blurred vision, burning eyes, faintness,
hypotension, shortness of breath, pruritus,
skin rash, dry mouth, bitter taste, excessive
salivation, anorexia, euphoria, depression,
slurred speech, confusion, restlessness,
hallucinations, and elevated SGOT, SGPT,
total and direct bilirubins and alkaline
phosphatase. Paradoxical reactions, *e.g.*,
excitement, stimulation and hyperactivity,
have also been reported in rare instances.

Dosage: Individualize for maximum beneficial
effect. *Adults:* 30 mg usual dosage; 15 mg
may suffice in some patients. *Elderly or
debilitated patients:* 15 mg initially until
response is determined.

Supplied: Capsules containing 15 mg or
30 mg flurazepam HCl.

Depend on highly predictable results with

Dalmane[®] (flurazepam HCl)

One 30-mg capsule *h.s.*— usual adult dosage
(15 mg may suffice in some patients).

One 15-mg capsule *h.s.*— initial dosage for
elderly or debilitated patients.

specifically indicated for insomnia

Objectively proved in the sleep research laboratory:

- sleep with fewer nighttime awakenings
- sleep within 17 minutes, on average
- sleep for 7 to 8 hours, on average,
with a single *h.s.* dose.



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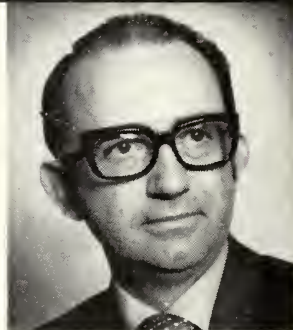
ROCHE LABORATORIES
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Nutley, New Jersey 07110

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complication or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

in purpose of drug information the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with an agency saying, "this information is generally agreed upon and before it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it should depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a longer one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could reserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

ly the doctor can remove that fear of 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebotrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

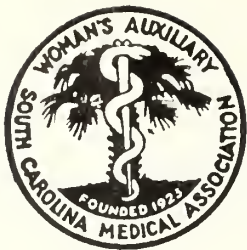
The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION

Each month in the SCMA Journal this year I will share with you, the physicians of our state, some items of interest concerning the Auxiliary.

Item: At the annual convention of the Woman's Auxiliary to the AMA in June in Atlantic City (meeting at the same time as the AMA Convention) the National Auxiliary's name was changed to AMA Auxiliary. There are male members of the Auxiliary, so "Woman's" was no longer appropriate. Woman physicians of South Carolina take note. Your husbands are welcome to become members of the State and National Auxiliaries.

Item: Mrs. Earle Wilkinson (Betty) of Tennessee was installed as President of AMA Auxiliary for 1975-1976. In her inaugural address Mrs. Wilkinson called for "a unity of purpose and goals in Auxiliary" with the theme for the year "Get it all together."

Item: At the AMA Auxiliary Convention in June the South Carolina Medical Auxiliary received an award for a contribution of more than \$15 per capita to the American Medical Association Education and Research Foundation Fund. The sum of \$16.84 per auxiliary member (\$18,524) was given to AMAERF in the 1974-75 year. Thank you for your help in this endeavor. To enable the Auxiliary to receive

credit for your donation to AMAERF, please use the AMAERF Fund Donation Form in the July issue of The Journal.

Item: Membership is a continuing challenge to the Auxiliary. In South Carolina there are approximately 1,500 members of the Medical Association but only 1,100 members of the Auxiliary. At the AMA Auxiliary Convention the South Carolina Auxiliary received an award for having organized a new county Auxiliary, Colleton County, in 1974-75. We still have 28 counties that do not have an organized county auxiliary. Our membership goals for this year are to gain 100 new members and two new county auxiliaries. You can help us by encouraging your spouse to become a member of a county auxiliary or a member-at-large. Members-at-large pay dues of \$8.50 to the State Treasurer, Mrs. George Smith (June), 320 Cherokee Road, Florence, S. C. 29501. Mrs. Rufus Cain (Elise), First Vice-President who is in charge of membership, will be happy to answer any questions regarding the duties and privileges of membership. Her address is: 1309 East Cleveland St., Box 951, Dillon, S. C. 29563.

Sara Shingler
President, WA-SCMA

CHARLESTON COUNTY AUXILIARY TO CELEBRATE 50TH ANNIVERSARY

The Charleston County Woman's Auxiliary will celebrate their 50th Anniversary on Saturday, November 1, 1975 at the beautiful Country Club of Charleston with a Gala Golden Champagne Evening.

The past presidents will be especially honored on this occasion for their devotion and contributions in making our fifty year history.

Our honored guests will be Governor and Mrs. James Edwards and our State President, Mrs. John Shingler, Jr. Other guests will also be recognized on this occasion.

A beautiful evening has been planned by the 50th Anniversary Committee Chairwomen, Mrs. Peter C. Gazes and Mrs. Sidney Seltzer. The evening will commence with a Champagne and Hors d'oeuvres Hour at seven o'clock. A strolling violinist will perform during this hour.

At eight o'clock an elegant seated dinner, which has been especially prepared for this occasion, will be served. The orchestra will play during this time for an evening of dining and dancing.

A lucky couple will win a week-end of their choice to Hilton Head just for being present for the drawing during the evening.

The Decorating Committee has some very special plans to make the evening a glittering, memorable event which no one will want to miss.

We are proud of our fifty years, and only hope our next fifty will be as fruitful.

The following notice appeared in the Thursday morning, March 13, 1924, edition of *The News and Courier*:

"Friday, March 14, 1924, 11:00 a.m.—

Meeting of Woman's Auxiliary to South Carolina Medical Association at home of Mrs. Robert S. Cathcart, 2 Water Street."

On Saturday following, March 15, 1924, a news item was headlined:

DOCTORS' WIVES MEET TO ORGANIZE

The article continued: "At a well attended meeting, held yesterday morning at the home of Mrs. Robert S. Cathcart, President of the Woman's Auxiliary to the South Carolina Medical Association, the doctors' wives of Charleston County were organized into an auxiliary to the county association and officers were elected as follows: Mrs. W. Atmar Smith, President, and Mrs. G. Fleming McInnis, Secretary. Mrs. Matthew S. Moore was elected a delegate to the State convention of the Medical Association to be held in Orangeburg, April 15, 16, and 17, and Mrs. Henry W. de Saussure was chosen alternate." Thus began the Charleston Branch, Woman's

Auxiliary to the South Carolina Medical Association.

Though there are not many records remaining of those early years, we know that Dr. C. F. Williams of Columbia was President of the South Carolina Medical Association and Dr. E. A. Hines of Seneca was Secretary and Treasurer. Dr. Hines had been instrumental in urging the formation of the State Auxiliary in 1923. There were eight districts in South Carolina and Charleston was placed in the First District along with the counties of Beaufort, Colleton, Berkeley, Jasper, and Dorchester. Mrs. H. M. Carter of Smoaks was the Councilor of the First District until 1926. Mrs. A. E. Baker of Charleston followed her as Councilor for one year and then became President of Charleston Auxiliary for 1927-1928. Mrs. W. G. Gamble, Jr., of Charleston was Councilor for 1927-1929, Mrs. W. W. Wild of North Charleston from 1929-1931, and Mrs. J. Sumter Rhame of Charleston 1931-1932.

The State Convention was held in Charleston on May 2, 1934, and the following is recorded: Mrs. Kenneth M. Lynch was named as Councilor of First District; Mrs. Robert Wilson, wife of the Dean of Charleston Medical College, gave the intro-

duction; and Mrs. Baker of Charleston graciously welcomed the Auxiliary to the city. Mrs. A. E. Baker was on the State Board as Chairman of Public Relations.

The aim of the Auxiliary, as set forth in the constitution and by-laws of the organization, was to extend the aims of the medical profession, through the wives of the doctors, to the various women's organizations which look to advancement in health and education; to assist at state, district, and county meetings; and to promote acquaintanceship among doctors' families that local unity and harmony may be increased. The Charleston Auxiliary emphasized the second portion of these aims and we find recorded the following:

In a letter written on February 24, 1940, to the State Auxiliary president by Pierre G. Jenkins, M.D.: "I am very glad to report to you at this time that the local Ladies Committee has just been organized and the general chairman is Mrs. Arthur M. Lassed, whose address is Windermere, Charleston, S. C."

The Convention was held in Charleston in 1940. Dr. Leon Banov was appointed to the Advisory Council to the State Auxiliary.

On March 13, 1941, a letter from Mrs. Cora Pollitzer, State President-Elect, to Mrs. H. L. Timmons, State President, records: "... I tried to persuade Mrs. A. E. Baker to reorganize the Charleston Auxiliary. She asked me to send her a letter listing the objectives of the Auxiliary and the reasons for its existence outside of its purely social feature."

Reorganization took place on December 4, 1946. Mrs. S. Harry Ross was State Auxiliary President and Dr. James McLeod was State Association President. Mrs. John A. Siegling was installed as Charleston County President with 35 paid members for the reorganization. Seven members were added during the year, and by 1947 membership had increased to 72. Mrs. Clay Evatt, who had been a charter member of the Greenville Auxiliary in 1927 and had served on the State Board

in 1929-1931, was a member of the Board of the reorganized Charleston Auxiliary. The convention was held in Charleston again on May 12, 13, and 14, 1948.

Since reorganization in 1946, there have been 29 continuous years of service to the medical profession in Charleston. There have been 27 Presidents and membership has increased to over two hundred. There have been many projects begun and completed, many projects begun and continuing. The aims and objectives have been reworded and expanded, but there still remains: "... through its members to extend the aims of the medical profession to all organizations which look to the advancement of health and education, to assist in the entertainment of South Carolina Medical Association conventions and to promote acquaintanceship among physicians' families that fellowship may increase."

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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THE SOUTH CAROLINA MEDICAL ASSOCIATION

COARCTATION OF THE AORTA—R. Randolph Bradham, M.D. and Edward F. Parker, M.D.

ACUTE EPIGLOTTITIS VS. ORGANOPHOSPHATE POISONING IN INFANCY: A CASE REPORT—Charles F. Wallace, M.D.

THE STATUS OF SUDDEN INFANT DEATH SYNDROME (1974), AND SIDS IN CHARLESTON COUNTY, SOUTH CAROLINA—Thaddeus J. Bell; Joel S. Sexton, M.D.; and Sandra E. Conradi, M.D.

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep under close observation of patients with addiction-prone individuals under care.

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For further information on this subject, the following references are provided:

1. Henry BW, *et al*: *Dis Nerv Syst* 30:675-679, Oct 1969.
2. Hollister LE, *et al*: *Arch Gen Psychiatry* 24:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics* 11:438-441, Sept-Oct 1970.

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider the fully pharmacology of agents employed; drugs such as phenothiazines, sedatives, barbiturates, MAO inhibitors and other antidepressants may potentiate sedation. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle



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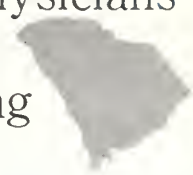
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ADVERSE REACTIONS: Drowsiness, fatigue, vertigo, incoordination, tremor, muscle weakness, ataxia, hypotension, respiratory depression, delirium and coma. Dryness of nose, mouth, and throat, pupillary dilatation or blurred vision, urinary retention, abdominal pain, nausea, vomiting, diarrhea, and hypersensitivity reactions. Overdose may result in hallucinations, excitement, ataxia, incoordination, athetosis, convulsions, and death.

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References—Should conform to the following order: surname and initials of author, title of article in small letters, name of periodical, with volume, page, month, day of month if weekly, and year—e.g., Lee, G. S. The heart rhythm following therapy with digitalis. Arch Int Med 44:554, Dec. 1942. They should be listed numerically in order of appearance in the text. Standard abbreviation for journals should be used. Note that periods are not used with these abbreviations as indicated by the Index Medicus. Other abbreviations should be standard—e.g., mg, ml, Gm.

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COARCTATION OF THE AORTA

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Coarctation of the aorta is a constriction, varying in the degree of occlusion, most commonly occurring below the left subclavian artery at the junction of the aorta with the ductus arteriosus. One need only to review the embryology of the aortic arch and its branches to understand the many variations that occur.

The etiology of coarctation of the aorta is poorly understood. Theoretically, there is the possibility that extension of the collagen rich, elastin poor, fibrous tissue of the ductus or ligament might cause constriction as the ductus is obliterated. There also exists the theory that in intrauterine life there is a slight shift in the point of separation of the blood streams to the upper and lower extremities and that this is sufficient to cause a decrease in the flow of blood through the aorta. Faulty development of the aortic arches is a possibility.

The old classification of preductal (infantile) where the coarctation occurs above the entrance of the ductus and postductal (adult) where it occurs below this point is not sufficient from a surgical viewpoint. It is necessary to consider them relative to associated hypoplastic segments of the aorta, cardiac anomalies, abnormalities of the branches of the aorta, aneurysms, amount of collateral circulation, and degree of narrowing. For instance, if the degree of narrowing is not great, collateral circulation poor, and there are present

weak but palpable femoral pulses, one need be concerned about obstruction of the aorta at the time of repair and the possibility of paraplegia as a complication. Whereas, if the degree of obstruction is marked with only a 1-2 mm opening, and there is good collateral supply to the distal aorta, clamping of the aorta is less likely to be hazardous.

Operative correction is indicated because of systemic brachiocephalic hypertension, aneurysm formation in the aorta adjacent to the coarctation and in the collateral vessels, cardiac failure, and the possibility of bacterial endocarditis. It is sometimes necessary to correct coarctation in infancy because of congestive failure and because of associated cardiac anomalies. For those that remain uncomplicated, the optimal age for correction is between eight and sixteen years. By the time a child reaches age eight, the aorta is usually an acceptable size for correction without the threat of recurrent coarctation because of a small anastomosis. Beyond this age, the individual becomes more susceptible to endocarditis and aneurysm formation, both of which can be the cause of rupture of the aorta.

Crafoord⁴ and Gross⁶ independently reported the first successful corrections of coarctation of the aorta in 1945. With improved equipment and more knowledge about the postoperative care of these patients, the mortality and morbidity have decreased markedly through the years.

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Diagnosis of coarctation is usually not difficult. Many subjects are asymptomatic and found to have coarctation because routine examinations reveal a systolic murmur, hypertension in the upper extremities, and a much lower blood pressure in the legs. Typical is the student who is found to be hypertensive on school exam. Femoral pulses are not palpable and a chest x-ray film shows rib notching. Infants and young children may develop congestive heart failure and cardiac enlargement. If the aorta above and below the coarctation is dilated, a "reverse 3" sign may be seen on the oblique or posterior-anterior roentgenogram of the chest. Rib notching is usually not present in infants. The electrocardiogram may be normal or may indicate left ventricular hypertrophy. Cardiac catheterization and angiography are usually not necessary to establish the diagnosis but may give valuable information about the character of the coarcted segment and other associated anomalies. Certainly, in an infant or young child with congestive failure, other causes such as valve defects and septal defects should be searched for.

During the past several years, we have been able to operate on patients at Roper Hospital with coarctation of the aorta as we have extracorporeal circulation available if needed during the procedure. A modest series of cases have been treated and have brought out some factors that warrant discussion. The patients are listed in Table I.

Coarctation in Adults

One of our most interesting patients was S. H., a 39 year old, white male admitted to the emergency room with complete A. V. dissociation, a slow ventricular rate, and seizures every five or ten minutes. An endocardial electrode was inserted transvenously immediately and temporary cardiac pacing established. He responded immediately and did well thereafter. Because of the nature of his residual conduction deficit, a permanent pacemaker was implanted. His history revealed that twenty years earlier hypertension was discovered but no treatment advised. He saw little of physicians in the interim because of good health. He was found to have brachiocephalic hypertension and further investigation by aortography confirmed a diagnosis of coarctation of the aorta complicated by an intercostal artery aneurysm (Figure 1). Both were repaired successfully and he has been relieved of hypertension.

Ostermiller and associates¹⁶ operated on 53 adult patients without a death and relieved hypertension in all patients. Levine and associates¹⁰ reported the successful treatment of a patient who was discovered to have coarctation of the aorta at age 63. She had developed a post-coarctation aneurysm which ruptured and sealed off sufficiently for successful resection to be accomplished.

Aneurysm Formation and Rupture

One thirteen year old child was referred hav-

TABLE I

<i>Year</i>	<i>Patient</i>	<i>Age</i>	<i>Repair</i>	<i>Complication</i>
1970	M. L.	15	Resection and graft	Pseudoaneurysm
1971	M. L.	15	Repair pseudoaneurysm	
1970	C. N.	21	Resection and primary repair	
1971	A. O.	13	Resection and primary repair	
* 1971	D. R.	13	Thoracotomy	Died
1971	R. P.	20	Resection and graft	
1971	M. W.	12	Resection and primary repair	
1972	S. H.	39	Resection and primary repair	
1972	R. K.	12	Resection and primary repair	
1972	S. S.	15	Resection and primary repair	
1973	S. H.	19	Resection and primary repair	
1974	D. J.	25	Resection and primary repair	
1974	T. L.	17	Resection and primary repair	

* See text

COARCTATION OF THE AORTA

ing been brought to the hospital in a moribund condition, in shock, with dilated fixed pupils. She was admitted to the neurology service and a chest x-ray film revealed mediastinal widening. The parents had been informed that the child had coarctation of the aorta previously and operative repair was advised. Although her condition appeared hopeless, an emergency operation was performed. The aorta proximal to the aneurysm had ruptured and the rupture was long, extending up the left carotid artery. No evidence of bacterial endocarditis was found and it was not clear whether an aneurysm had actually formed or not. She died on the operating table from exanguination and cerebral insufficiency.

Nikaidoh, Idriss, and Riker¹⁴ reported three cases of aortic rupture in children ages five, seven, and ten which were associated with coarctation of the aorta. Two of the patients died of hemorrhage, one with mycotic aneu-

rysm during operation, and the other with dissection before operation could be performed. The remaining patient survived operative repair after a very complicated postoperative course. Khazei and Cowley⁹ reported two cases of mycotic aneurysm complicating coarctation of the aorta and reviewed the literature. They found approximately one-fourth of the aneurysms superimposed on coarctation to be mycotic and most often located distal to the stenosis. Hemolytic or non-hemolytic streptococcus was the most common infecting organism but other bacterial agents were frequently encountered. In the series reviewed, the mortality rate was approximately 100 per cent unless proper therapy was instituted. Prompt surgical intervention after six weeks of intensive antibiotic therapy was advised. Oldham and associates¹⁵ reported one case of a five year old boy successfully treated by resection following six weeks of antibiotic therapy. Lui¹¹ reported a very unusual case of a multisaccular aneurysm of the proximal descending thoracic aorta associated with a coarctation that he believed to be congenital in origin. Other etiological factors were absent.

Mirza, Hassan, and Jordan¹² reported the extremely unusual case of spontaneous rupture of the abdominal aorta following resection of a coarctation of aorta. The patient was a nine year old boy who underwent resection of the coarctation and an end-to-end anastomosis. He complained of abdominal pain on the second postoperative day and became hypotensive on the third postoperative day. Laparotomy revealed rupture of the abdominal aorta just above the bifurcation and there was only a 0.5 cm tissue bridge remaining between the two ends. The patient died and postmortem exam revealed hypoplasia of the distal abdominal aorta and iliac arteries.

Postoperative Paradoxical Hypertension

One of the most dreaded yet fascinating complications following resection of coarctation of the aorta is that of paradoxical hypertension, first described by Sealy, Harris, Young, and Calloway in 1957.¹⁹ They found that a significant elevation of blood pressure might develop immediately after operative correction of coarctation and regress in 36 hours and was not clinically significant. However, a delayed hypertension, principally diastolic, may occur on the second to fourth postoperative day some-



Figure 1. Chest x-ray film of patient, S. H., showing: (1) implanted pacemaker, (2) aneurysm of intercostal artery, (3) coarctation of thoracic aorta, and (4) dilated internal mammary artery.

times in association with abdominal pain. Small bowel necrosis occurs secondary to an arteritis of vessels below the coarctation site. In a later article, after more experimental and clinical data had accumulated, Sealy¹⁸ reported that this delayed, life-threatening hypertension was likely due to a complex relationship of reflexes from the baroreceptor area, a norepinephrine increase, and local changes in blood vessels below the coarctation as a result of adaptation to the coarctation.

Ibarra-Perez and Lillehei⁸ reported on the treatment of mesenteric arteritis following resection of coarctation of the aorta. Thirty-eight of 331 survivors of resection of coarctation were paradoxically hypertensive in the post operative period. Thirty-four had abdominal pain. Twenty-eight of the hypertensive patients received antihypertensive treatment. Of these, one died. Therapy had been delayed. Ten patients did not receive antihypertensive treatment. Two of these underwent laparotomy for mesenteric arteritis and one died. The authors strongly advise that antihypertensive drugs should be started early after the onset of the hypertension and pain in adequate dosage to control both. They also advise low molecular weight dextran, gastrointestinal decompression, and antibiotic therapy as adjunctive therapy.

Verska, DeQuattro, and Wooley²¹ reported an incidence of 50 per cent occurrence of paradoxical hypertension in 22 consecutive patients having resection of coarctation of the aorta. They found a higher incidence of increased excretion of catecholamines in the hypertensive group and thought this might be one factor causing this phenomenon.

In our series of patients, we have had one patient, P. J., who developed marked immediate hypertension but none have had the delayed form and none have had significant abdominal pain postoperative.

Pseudoaneurysm Postoperative

One of our patients, M. L., developed a pseudoaneurysm postoperative resection of a coarctation and insertion of a graft (Figure 2). It was believed that this was caused by disruption of a few sutures as only a small defect was found in the anterior part of the upper anastomosis. Several buttressed, mattress sutures repaired the defect satisfactorily.

Callard, Wright, Wray, and Minor³ successfully treated a 22 year old woman who developed false aneurysms at both ends of a graft used to repair a coarctation of the aorta. This was caused by an infection with an opportunistic fungus, a species of *Mucor*. Resection, regrafting, and treatment with amphotericin B cured the infection.

Gazzaniga⁵ reported a case of the formation of a pseudoaneurysm subsequent to the unsuspected total distraction of the aorta proximal to a previously resected coarctation. The site of disruption appeared to be at the point where a vascular clamp had been applied during the repair. The patient underwent successful aortic reconstruction during intermittent left heart by-pass.

Spinal Cord Complications

One of the most dreaded complications following repair of coarctation is paraplegia. Predominant factors considered as cause for



Figure 2. Chest x-ray film of M. L. showing: (1) outer edge pseudoaneurysm, (2) graft, compressed by pseudoaneurysm.

this have been the number of intercostal arteries ligated and the period of cross-clamping of the aorta. Fortunately, in our small series, we have not had this complication.

The most informative article on this subject was published in 1972 by Brewer, Fosburg, Mulder, and Verska.¹ They collected 12,532 cases of coarctation repair from leading thoracic surgeons and found that there were 51 cases of spinal cord complications. Fifteen more were collected from the literature giving a total of 66 cases for a retrospective study. It is interesting that in the report there were a total of eight additional cases that had spinal cord complications without operation. These are believed due to pressure of an intercostal artery aneurysm on the anterior spinal artery or the cord itself, or rupture of an intercostal aneurysm with formation of a hematoma. Bryant,² in discussion of Brewer's paper, described one such case that had return of neurological function following repair of a coarctation.

Included in Brewer's and associates' investigation was a reassessment of the anatomy of the spinal cord blood supply. They found the former concept of segmental blood supply to the cord by multiple radicular branches from the intercostal vessels to be erroneous. Many variations were found in the anatomy of the anterior spinal artery and cord supply by the intercostal vessels.

In summary, these authors also found that neither sacrifice of intercostal arteries nor the time of occlusion of the aorta was related to spinal cord injuries in all cases. Sufficiency of collateral circulation must be verified at operation. The most reliable test is measurement of pressure above and below, before and after occlusion. Either hypothermia, left heart by-pass, or a jump graft should be utilized if pressure in the distal aorta is not considered adequate for perfusion. The variation of the blood supply to the anterior spinal artery may not permit even the briefest cross-clamping, even though the collateral circulation has been adequate by testing and protective measures have been employed. The authors advise that since this complication may occur despite all measures to prevent it, the patient should be so informed before operation.

Hughes and Reemtsma⁷ record pressures in the distal aorta before and after occlusion. If the mean pressure in the distal aorta is below 50 mm Hg, left heart by-pass is instituted

and maintained during the repair.

Technique of Operative Repair

Our preference for repair of coarctation is excision of the coarcted segment and primary repair if the two ends come together without much tension. This often requires mobilization of the distal aorta and intercostal arteries almost to the diaphragm and mobilization of the arch proximally. Rarely was any intercostal artery divided in our cases. Only two of the eleven cases required an interposing graft. The cardiac by-pass apparatus and technician are in the room and available if it is determined that distal perfusion seems inadequate. A femoral vein to femoral artery by-pass technique would be used.

Recently, the patch graft technique has been popularized by Moor, Ionescu, and Ross¹³ and by Reul, Kabbani, Sandiford, Wukasch, and Cooley.¹⁷ Although, this is a good operation to use in certain selected cases, it is not our primary choice of procedure if a primary end-to-end anastomosis can be accomplished. We do not like to reconstitute the aorta with a foreign body if this can be avoided.

Siderys, Graffis, Halbrook, and Kasbecker²⁰ used a large by-pass graft in a 46 year old woman who had coarctation of the aorta. The site of coarctation was inaccessible because of a fibrothorax. The graft was constructed from the ascending aorta to the infrarenal abdominal aorta.

Summary

A modest series of patients having repair of coarctation of the aorta have been presented as a basis for discussing factors that are important in diagnosis, treatment, and management of complications that might occur before and after surgical correction. For those not complicated, surgical repair is recommended between ages eight and twelve years. The hazards of waiting longer are discussed and illustrated by complications developing in two of our patients. Postoperative paradoxical hypertension and spinal cord impairment are two dreaded complications. The former can usually be managed successfully if recognized early. The latter can usually be prevented by measurements of distal aortic pressures during operation, avoiding obstruction of collateral circulation, and instituting flow to the distal aorta while cross-clamping the aorta during repair. The technique of repair is discussed. □

COARCTATION OF THE AORTA

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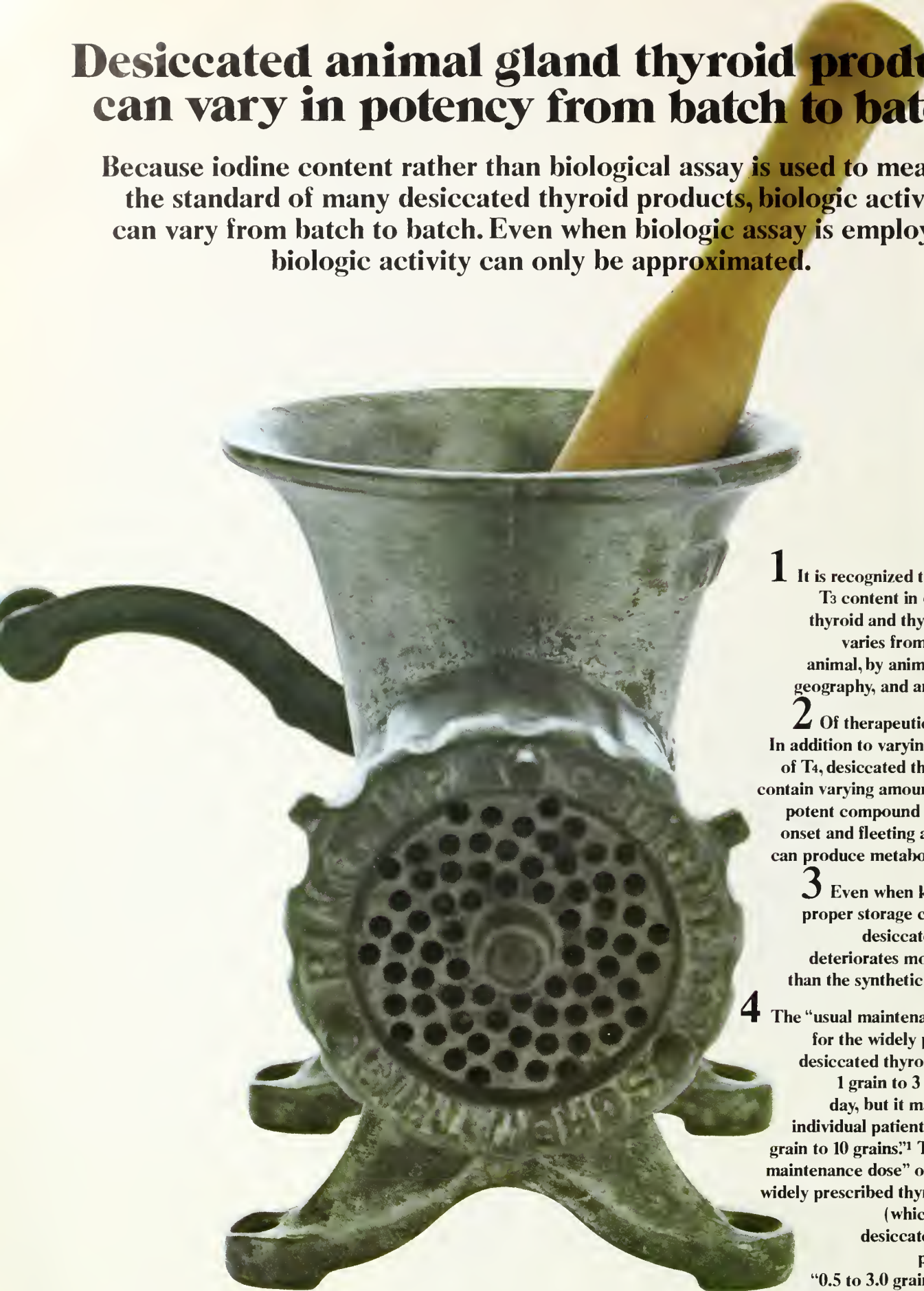
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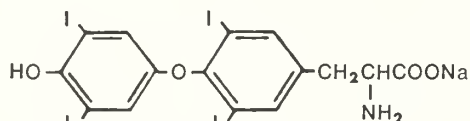
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Contraindications

There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis. (See WARNINGS)

Warnings

Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions

Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule. With SYNTHROID (sodium levothyroxine) Tablets, the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

Adverse reactions

Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration

For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0.2 mg) of SYNTHROID (sodium levothyroxine) Tablets daily will restore normal thyroid function and only occasionally will patients require larger doses. Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism. Special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent onset of hypothyroidism, full replacement dose of 150 mcg (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view of the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patient as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedematous infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 mcg (0.025 mg) per day. Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at three to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration.

Laboratory tests to monitor thyroid replacement therapy are of limited value. Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with the clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occurs and should not be considered evidence of overdosage per se.

In all cases, clinical impression of the well-being of the patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critical importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size, the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROID Injection may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsiveness within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred. Like the oral dosage form, SYNTHROID Injection produces a predictable increase in the circulating level of hormone with a long half-life. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient is fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

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ACUTE EPIGLOTTITIS VS. ORGANOPHOSPHATE POISONING IN INFANCY: A CASE REPORT

CHARLES T. WALLACE, M.D.*

Respiratory distress and/or failure in infancy is a common, frightening syndrome with multiple etiologies (see Table I). Acute epiglottitis and organophosphate poisoning are rare causes of this syndrome in early infancy. This is a report of an infant who was diagnosed and treated for acute epiglottitis at age 3 months and organophosphate poisoning at age 5 months.

Admission Number One

This three month old white male infant developed respiratory distress while playing with his father. He exhibited dyspnea, retractions and cyanosis. He then became cold and clammy and was taken immediately to the emergency room where apneic episodes occurred. He was given oxygen, and after initial examination, transferred to the Medical University Hospital. Significant past medical history revealed Ampicillin therapy for pneumonia two weeks previously and intimate contact with a child who died three days earlier of acute epiglottitis. There was no history of allergy or poison ingestion. Physical examination revealed a temperature of 98.6°F. His skin was pale, cool and clammy. Respirations were rapid and shallow at 60 per minute with moderate retractions. Heart rate was above 200/minute. Blood pressure was 100/65 torr. Pupils were extremely pinpoint. There was a copious mucous discharge from the nose. Examination of the epiglottis revealed it to be pale and large. There was nasal flaring with intercostal, subcostal, and supracostal retractions. Expiration was prolonged with scattered wheezing. Bowel sounds were active.

Neurologic examination revealed deep tendon reflexes 2+ bilaterally. A chest roentgenogram was negative. Blood studies revealed a hemoglobin of 9.6gm/100ml, hematocrit of 28.1%, and a white blood count of 10,400. Throat cultures were obtained and later reported as negative. Arterial blood gas analysis and lateral neck roentgenograms were not performed. The infant was intubated orotracheally with a 3.0mm endotracheal tube after failure to improve with oxygen administration. The intubation was somewhat difficult due to trauma of the upper airway caused by repeated examination and attempted intubation by other physicians. Following intubation a tracheostomy was performed under general anesthesia. The infant remained apneic after the tracheostomy and required mechanical ventilation with oxygen over night. He was weaned from the respirator 12 hours post-operatively. His remaining hospital course was unremarkable except for diarrheal stools, copious airway secretions and one episode of cyanosis and respiratory distress. His trachea was decannulated seven days after admission, and the infant discharged the following day.

Admission Number Two

Two months later, the infant again suddenly developed respiratory distress. He had vomited 3 times the day before and had had diarrhea for the past twenty-four hours. Physical examination revealed a well-developed white male child who was pale, limp, and gasping. There were copious secretions in the nose and upper airway. Pupils were extremely pinpoint. Respiratory rate was 60/minute, shallow, and characterized by severe retractions. Coarse rhonchi were present bilaterally. Heart rate was 160/minute. Examination of the oropharynx revealed a large, pale epiglott-

TABLE I¹

COMMON CAUSES OF ACUTE RESPIRATORY FAILURE IN INFANTS (1 to 24 Months)

Bronchopneumonia
 bacterial
 viral (bronchiolitis)
 aspiration
Upper Airway Obstruction
Congenital Heart Disease
Status Asthmaticus
Septicemia

Foreign Body Aspiration
Intrathoracic anomalies
 diaphragmatic lesions
 vascular ring
 lobar emphysema
Encephalitis
Poisoning
Cystic Fibrosis

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ACUTE EPIGLOTTITIS

TABLE II

TIME	DRUG	PUPILS
6:20 P.M.	Atropine 0.2 mg. I.V.	pinpoint
6:30 P.M.	PAM 200.0 mg. I.V.	
6:35 P.M.	Atropine 0.2 mg. I.V.	
6:50 P.M.	Atropine 0.2 mg. I.V.	
7:05 P.M.	Atropine 0.2 mg. I.V.	
7:20 P.M.	Atropine 0.2 mg. I.V.	dilated
8:05 P.M.		dilated
9:00 P.M.	Atropine 0.2 mg. I.V.	dilated

tis with normal appearing glottis and vocal cord movement. Complete blood count, electrolytes, B.U.N., and blood glucose were within normal limits. A chest roentgenogram was interpreted as being consistent with bronchiolitis. An arterial blood gas analysis revealed a pH of 7.4, PaCO₂ of 37 torr and PaO₂ of 77 torr. Further questioning of the parents revealed that the mother had sprayed their trailer home with "Raid" brand roach and ant killer the previous night. "Raid" contains an organophosphate poison among its contents. In view of this, blood cholinesterase levels were obtained, after which atropine was given in intravenous increments until a total dose of 1.7mg. had been given over 3 hours (see Table II). One dose of PAM was also administered. The infant became responsive, cried vigorously, and regained good muscle tone within 90 minutes of therapy. He was hospitalized overnight and discharged home the following morning. Serum cholinesterase was 1.22 units (normal is 2.22), and red blood cell cholinesterase 5.11 units (normal is 11-16).

Discussion

Acute epiglottitis occurs less than one percent of the time in infants less than 6 months of age, and is more common in the one to four year old age group.^{2, 3} Fever and respiratory distress of rapid onset and progression are characteristic of this disease (see Table III). *Haemophilus Influenza* is the most common causative organism. A positive diagnosis is made with lateral neck roentgenograms, and possibly, direct examination of the epiglottis. Examination of the epiglottic area may lead to complete respiratory obstruction. The treatment of acute

epiglottitis is early placement of an artificial airway. Whether a nasotracheal or tracheostomy tube is best is controversial at present.^{2, 4}

Poisoning, while also unusual in early infancy, remains a major cause of accidental death in pediatric patients. Most cases of poisoning in infancy result from self-ingestion or accidental administration by a sibling or friend. Organophosphate intoxication is one of the most unusual types of poisoning. It differs from other poisons in that (1) it may be absorbed by virtually any route, including skin, conjunctiva, respiratory and digestive tracts, and (2) the effects are usually reversible if detected in time.⁵ Unfortunately, the diagnosis may be missed or delayed because a history of exposure is not readily apparent in infants and young children.⁶ The signs and symptoms of organophosphate poisoning are listed in Table IV. Treatment involves cardiopulmonary support, tracheo-bronchial toilette, and pharmacologic antagonism with atropine and pralidoxime (PAM).

In retrospect, this infant's two illnesses were most likely of one and the same origin: organophosphate poisoning. Attempts to contact this infant's parents for further questioning concerning the events preceding the first admission have been unsuccessful.

TABLE III 2, 3
SIGNS AND SYMPTOMS OF ACUTE EPIGLOTTITIS

Respiratory Distress	Upper Respiratory Infection
Fever	Hoarseness
Rapid Onset and Progression	Drooling
Cough	Cyanosis
Swollen, cherry red epiglottis	Strider
Positive Lateral Neck Roentgenogram	Sore Throat

ACUTE EPIGLOTTITIS

TABLE IV⁵
SIGNS AND SYMPTOMS OF ORGANOPHOSPHATE POISONING

<i>Muscarinic Manifestations</i>	
Bronchial Tree	Wheezing, dyspnea, increased bronchial secretion, cough, pulmonary edema, cyanosis
Gastrointestinal System	Vomiting, abdominal cramps, diarrhea, fecal incontinence
Sweat Glands	Increased sweating
Salivary Glands	Increased salivation
Lacrimal Glands	Increased lacrimation
Cardiovascular System	Bradycardia, hypotension
Pupils	Miosis, occasionally unequal
Ciliary Body	Blurring of vision
Bladder	Frequency of urination, urinary incontinence
<i>Nicotinic Manifestations</i>	
Striated Muscle	Muscle twitching, fasciculation, cramp, weakness, including muscles of respiration
Sympathetic Ganglia	Pallor, tachycardia, hypertension
<i>Central Nervous System Manifestations</i>	
	Restlessness, emotional lability, tremor, drowsiness, confusion, slurred speech, ataxia, generalized weakness, coma with absence of reflexes, Cheyne-Stokes respiration, convulsion, depression of respiratory and circulatory centers

Summary

The purpose of this report is not to criticize patient management or focus attention on a misdiagnosis, but (1) to emphasize the problems encountered in management of acute respiratory distress in infancy, and (2) to alert the physicians in our state to the possible misuse of household insecticides.

Respiratory distress in infancy is potentially a rapidly progressive process which may end in acute death of an individual who should have

a long productive life.⁷ The evaluation and treatment of infants with this syndrome require a thorough history and physical exam, careful monitoring and cardiopulmonary support, immediate and proper diagnostic studies, prompt and diligent teamwork, and expert intensive care.

Finally, safe transport systems with individuals trained in management of airway disease must be devised. □

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THE STATUS OF SUDDEN INFANT DEATH SYNDROME (1974), and SIDS IN CHARLESTON COUNTY, SOUTH CAROLINA

THADDEUS J. BELL.*

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As a third year medical student at the Medical University of South Carolina, I decided to take a rotation in Forensic Pathology (one of the few offered in the country for medical students). During the course of this rotation, I became intrigued with a phenomenon called the "Sudden Infant Death Syndrome." I became interested in this syndrome (SIDS) as it is a disease entity that snuffs out the life of predominately black and Indian infants with no apparent cause and inflicts psychological trauma on the parents and family.

History

The pediatric aspects of forensic pathology have developed markedly during the past two decades from almost zero to the present intense interest in two syndromes, the "battered child" and "sudden infant death." In this regard Knight stated: "The first is more genuinely within the true province of the medicolegist having direct criminal, psychiatric and even penological aspects. The second is almost purely a scientific problem, and until recently, was left in the lap of the forensic pathologist, not because of any legal or criminal connotations but because no other medical specialty became involved."¹

SIDS is not a new disease. At present SIDS is the leading cause of mortality among infants more than a month old. There is some evidence that SIDS has been known since antiquity. The sudden death of an infant is referred to in the Old Testament (I King, 3:19-20 — "and this Woman's child died in the night because she overlay it").^{2, 3}

In 1892, a Scottish physician, C. Templeman, wrote perhaps the first significant article on

SIDS. He attributed the death of 258 infants to suffocation and ascribed the cause to carelessness of the parents.⁴ SIDS was little discussed and poorly investigated until the middle of the 20th century.

The primary reason for the lack of interest among doctors and scientists had to do with the nature of the disease. Until recently, SIDS cases went directly from their homes to the morgue and no postmortem examinations were performed.⁵ Not until the early sixties did the medical research community begin to give SIDS serious attention. Although the age-old problems of many childhood diseases (e.g., diphtheria, whooping cough, scarlet fever, polio and smallpox) are preventable and have been virtually eliminated, little is known of the etiology and pathogenesis of SIDS. At the Second International Conference on Cases of Sudden Death in Infants (commonly known as "crib death" or "cot death"), this syndrome was described as "The sudden death of any infant which is both unexpected by history and where a thorough necropsy examination fails to demonstrate an adequate explanation for death."⁷

According to Bergman (1973) the most consistent epidemiologic evidence on SIDS to date indicates that throughout the world SIDS occurs once in every 350 births. In the United States, SIDS causes about 10,000 infant deaths each year, approximately 2-3 deaths of every 1,000 births, or almost one sixth of all infant mortalities. SIDS kills more infants between the ages of one week and 12 months than any other disease and is second only to accidents as the cause of death in children between one week and 15 years of age. About 90 percent of the SIDS cases occur between two weeks and six months of age, with a peak incidence between two and three months. Most of the re-

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Ragan, C. The Clinical Picture of Rheumatoid Arthritis in Arthritis, ed. 8, edited by J. L. Hollander and D. J. McCarty, Jr. Philadelphia, Lea & Febiger, 1972, chap. 21, p. 335.

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Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals. Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug, its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

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SIDS IN CHARLESTON COUNTY

maining cases occur before the first birthday but "classic" SIDS can occasionally strike infants beyond the age of one year. It occurs most frequently in the winter months.^{2, 3, 8, 9, 10, 11}

In a recent study of 950 SIDS, Raven reported that this syndrome is significantly greater in infants born to nonwhite than to white mothers, and especially to premature infants of unwed mothers. She concluded, as have others, that low birth weights, congenital defects and high risk mothers are associated with SIDS. She also postulated that the same factors which influence the incidence of crib deaths also affect the incidence of fetal and neonatal deaths and noted that the season incidence of SIDS studies coincided with an paralleled deaths due to atypical pneumonia.¹³

Although this syndrome afflicts predominant infants of a poor socio-economic environment, it can occur in children of any social economic background. Unexplained racial differences occur. The lowest rate of occurrence is among orientals, followed by whites, Mexican Americans, and blacks with the American Indians having the highest incidence according to Valdes-Dapena's Study.¹⁴

Bergman stressed that in his study the sudden infant death syndrome occurred in infants who were previously in good health. Sometimes they have been reported to have had a minor respiratory infection. Statistically, death occurs between midnight and 6 a.m. and every proven case occurred during sleep. Often these infants have been seen prior to death and declared to be in good health by their physician. It is important to note that when death does not occur during sleep, other causes should be suspected and searched for. Often the question of cries or sounds made by the baby before death is asked about by investigators. Even when the baby is in close proximity to members of his family, noises have not been reported prior to death.² Often SIDS victims are found in the same position that they were in, when last seen alive. However, this does not have to be the case. Infants are discovered in various positions.¹⁵ Sometimes they are seen with blankets pulled over their heads. This finding led to the common misconception that the child smothered to death or suffocated.² Wooley conclusively demonstrated that covering the face of infants with ordinary bedding is insufficient to cause anoxemia. Even a very young

infant can turn or lift his head to find air space, and blankets found in cribs are often made of woven fibers through which air easily passes.¹⁶ At the death scene, sometimes blood-tinged froth can be seen in the nostrils and mouth of the victims. Parents often think this is the result of internal hemorrhage, when in reality it is due to hemorrhagic pulmonary edema.²

Local Study

From January 1973 to October 1974, under the newly established medical examiner's system, a clinical diagnosis of SIDS was reported and confirmed in 16 infants out of 5500 (estimate) births in Charleston County, South Carolina. The greatest number of deaths occurred in March. The age range of these infants was from 3 weeks to 15 months. There were 6 black males, 4 white males, 6 black females and no white females. Eight children were reported to have had a minor respiratory infection prior to death. The remaining eight were reported to be free of any respiratory infection. Congenital defects and pneumonia were the primary etiologies of death in 10 other cases of infant death reported during the same time period. These findings correlate with the above quoted figures and point out that really meaningful studies must be long range or incorporate a number of reporting medical examiners systems in order to have enough cases to be significant.

Disposition of Suspected Case

In making a diagnosis of SIDS a prompt autopsy by a trained pathologist should always be performed. However, this is often not possible. In cases where the clinical findings are typical (age range, previously well infant who died during sleep, etc.) the diagnosis of SIDS can be made with a reasonable amount of certainty. It is absolutely essential that an obviously lethal lesion not be present in order for the death to be attributed to SIDS.² Bergman reported that in 15 per cent of sudden, unexpected infant deaths, a definite cause of death other than SIDS was found. Meningococcemia, subdural hemorrhage and myocarditis headed the list. Confirmatory postmortem evidence (autopsy, chest x-ray films, blood cultures, toxicology reports, etc.) is recommended to rule out pneumonia, septicemia, central nervous system hemorrhage and drug overdose.²

Autopsy Findings

The following observations are typically

found at autopsy: Petechiae often cover the pleural surfaces of the lungs, epicardium and thymus. Characteristic petechial hemorrhages of the thymus are almost always limited to the thoracic portion of the structure. The blood is largely fluid and does not clot. The mucosa of the larynx, trachea and bronchi are often very congested. Slight inflammation of the air passages is often evident. The tracheobronchial and cervical lymph nodes are usually hyperemic. Visceral congestion is usually seen. The tonsils show little gross change. The presence of curdled milk in the stomach is not unusual. The urinary bladder in most cases is empty.

Etiology

The etiology and basic mechanism of SIDS have not been firmly established. Many of the theories as to the etiology of SIDS have been completely discarded by many investigators such as milk allergy, immunoglobulin deficiency, cold injury, bacterial infection, epidural hemorrhage and stress.^{2, 14}

Of the 950 cases of unexpected infant deaths studied by Raven, 71.8 per cent of the cases studied were associated with an acute respiratory infection — primary acute interstitial pneumonitis. Other causes of sudden death in infants originally suspected to be SIDS death were bronchopneumonia (5.6%), miscellaneous bacterial and viral infections (5%), congenital heart disease (4.6%), suffocation (4.6%) and multiple congenital defects (2.8%).¹³ In Bergman's studies, 44 per cent of the infants studied had a history of respiratory infection.² A number of common viruses (adenoviruses, coxsackie, parainfluenza, Rhinoviruses, polio viruses) have been recovered from autopsy from different anatomic sites in SIDS infants, but to date attempts to link a viral etiology to the SIDS have been unsuccessful.^{2, 3, 7, 8, 14}

Recently new leads have been developed but a few of them are leads that are expected when an unexplored field is searched. Perhaps the most important observation in recent years is that of Steinschneider who observed that normal infants two to three months old tend to have apneic periods during sleep and that these episodes are more prolonged when the infant has upper respiratory infections. He has also documented recurrent periods of spontaneous prolonged apnea in infants who subsequently died suddenly and unexpectedly. Autopsy seldom reveals the cause of death in these in-

fants.¹⁸ Unger, in a separate study, has reported similar findings.¹⁹

Naeye demonstrated hyperplasia of smooth muscle of small pulmonary arteries in SIDS infants as compared with that of controls. Such changes resemble those present in normal infants and children living at high altitudes and may result from chronic hypoxia. Perhaps as Valdes-Dapena suggested, the changes are related to the prolonged periods of apnea reported by Steinschneider.¹⁴

Beckwith, Ray and Bergman suggested that laryngospasm may be responsible for death in SIDS. These investigators explain, "the terminal event of SIDS is laryngospasm, mediated through the autonomic nervous system and triggered by viral inflammatory disease of the upper respiratory tract."² Substantial proof of this theory is still lacking.^{2, 14}

Shaw suggested that these infants died because they are obligatory nose breathers. He also suggested that the infants die from anoxia during temporary nasal plugging with mucus because they will not breath through their mouths.^{2, 20} This theory has met with disagreement because obligatory nose breathing characterizes the neonate rather than the infant at a susceptible age for SIDS and because post-mortem radiologic studies have demonstrated clear air passages of SIDS infants.^{2, 14} Absence or insufficiency of Vitamin E and cervical spinal cord hemorrhage have been suggested as related to SIDS but have been disproved.¹⁴

Physician's Responsibility to Parents

Hoekelman has outlined the physician's specific responsibilities to the family of the SIDS infant. First and foremost, a home visit should be made by the physician, as soon as time permits, to observe the environment and the circumstances in which the death occurred and to begin the process of educating and reassuring the parents. At the time the physician confirms the death of the infant, it should be stressed to the parents that a complete autopsy should be performed to rule out infection and a danger to the rest of the family or congenital anomalies which may be hereditary. It should be stressed that the coroner or medical examiner may want to order an autopsy with or without family permission. Since 15 per cent of infants reported as SIDS die of specific causes, it is important that a SIDS diagnosis not be given to the parents until after the autopsy has been

completed.^{2, 21} The physician should assure the family that he will personally explain the results of the autopsy to them. Usually this is within 6 to 12 hours. If, in fact, the findings are in line with SIDS, the parents should be told that their baby died of a definite disease entity (SIDS) and that in light of present knowledge death was unavoidable. There is evidence that in the majority of SIDS cases parents are not given information and that pediatricians and family practitioners seldom are involved in the management of the after effects of this tragedy. The last responsibility that the physician has to the family takes place about a month later. At this time, if the physician deems it necessary, he should relate to the parents any pertinent autopsy findings, answer questions and discuss

the fact that SIDS is not hereditary and should not hinder plans for future pregnancies.²¹ Bergman reported in a study of 421 SIDS cases that occurred in 148 communities in 47 states that only half of the 421 parents interviewed were correctly informed that their babies had died of crib death. His studies also indicated that families more likely to be given information were prominent and white. Black parents were four times as likely to be given inadequate information about the cause of death.⁵ It is only through thorough investigation of these deaths by a medical examiner's system and education and counseling of the parents by a physician that misconceptions, unfounded criminal actions and grave psychological damage to the parents can be avoided.

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SUDDEN INFANT DEATH SYNDROME

Progress Report

JOSEPH C. MOORE, JR., M.D.*

Prior to 1963 Sudden Infant Death Syndrome (SIDS) was a recognized but ill-defined clinical entity. The First International Conference on the subject of sudden death in infancy marked the beginning of a significant united effort to study this terrifying and fascinating phenomenon. Since that time much has been written on the subject and more research is being done now than ever before. Although no definite etiology has yet been elucidated for SIDS, also known as crib death, several promising areas have recently been uncovered. Organized parent groups must receive much of the credit for the recent interest in the syndrome and availability of research funds. It will be the purpose of this paper to review some of the most recent advances in the study of SIDS.

SIDS is currently defined as "the sudden death of an infant or young child, unexpected by history, in which a thorough postmortem examination fails to demonstrate an adequate cause for death."¹ It is essential that this definition be strictly adhered to.

Approximately 10,000 crib deaths occur annually in the U.S.; the greatest incidence being in infants one to four months of age. This is the leading cause of death among infants between one week and one year of age, the incidence being about three per thousand live births. The victims are generally normally developed and well-nourished. Approximately one-third are born prematurely. Recurrences in the same family are relatively common, an observation that often leads to speculation about hereditary predisposition. The incidence is higher with lower socio-economic groups, low birth weight babies, mothers less than twenty years old, and mothers who have had little or no prenatal care. Crib death is more apt to occur during the late winter and early spring and may be preceded by a mild respiratory infection.

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Most infants die in their sleep and are found dead in the early morning hours; relatively few collapse while someone is in attendance. Deaths also occur in hospitals among treated babies about to be sent home. These are generally infants who have suddenly, silently, and without struggling, stopped breathing and are subsequently resuscitated. Each such infant who is brought to the emergency room presents quite a problem, as among the few that are discharged, a certain number return dead within a week or so. Should all such infants be admitted then and monitored, or should parents monitor them? Valdez-Dapena, who has written as much on SIDS as anyone, feels that this question cannot currently be answered.²

Postmortem examination is characteristically unrewarding. Commonly petechiae in thoracic organs, slight or moderate pulmonary edema and congestion, and irregularly aerated and focally emphysematous lungs may be seen. Histologic examination often shows mucosal necrosis and ulceration in the larynx and minor degrees of inflammation in the tracheo-bronchial tree. Inflammatory changes in the lungs are usually negligible. Minor degrees of meningitis and enteritis are encountered. There may be spinal epidural hemorrhage. In short, the findings are inadequate to explain the child's death.

A variety of etiologic factors have been postulated in recent years for crib death, but few of these have been substantiated with convincing evidence. Hypersensitivity to cow's milk and subsequent anaphylaxis has been refuted,¹ as have myocardial conduction irregularities³ and immunologic deficits.² Laryngospasm, lack of vitamin E or selenium, metabolic or genetic defects, parathyroid or adrenal insufficiency, hypocalcemia, and lack of potassium or calcium in the myocardium have been disproven.² Suffocation by bed-clothes is no longer seriously considered.

One currently popular and promising area of

SUDDEN INFANT DEATH SYNDROME

study concerns the effects of viral infection. Several investigators have shown a significantly increased rate of isolation of common viruses from various anatomic sites at necropsy. Except for the upper airway, however, histologic sections give no morphologic evidence for infection. Additionally, there is no evidence for overwhelming viremia.

Certain circumstantial evidence, however, strengthens the case for infectious etiology. Minor respiratory and gastrointestinal signs and symptoms frequently precede the fatal event. Other family members may have also had a cold or whatever ailment was prevalent at the time. Certainly more work needs to be done in this area.

Perhaps the most important observation in recent years is that of Steinschneider,⁴ who has found that normal infants two to three months old tend to have apneic periods during sleep and that these periods are more prolonged during upper respiratory infections. Prematurity, a predisposing factor in SIDS, was also shown to be associated with a significantly increased amount of prolonged apnea during the first few weeks of life. Additionally, Steinschneider has documented recurrent periods of spontaneous prolonged apnea in infants who subsequently died of crib death. He postulates that prolonged apnea, a physiological component of sleep, is part of the final pathway resulting in sudden death and that upper respiratory infection and prematurity are predisposing factors. Additionally, he feels that infants at risk might be identified prior to the final tragic event.

Naeye⁵ has demonstrated significant thickening in the walls of small pulmonary arteries in affected infants as compared to controls.

These changes are similar to those present in normal infants living in high altitudes and suggest to him the effects of chronic hypoxia. He feels that these findings may be related to the aforementioned episodes of prolonged apnea.

The fact that intrathoracic petechiae are the most consistent postmortem finding in SIDS has suggested to some that upper airway obstruction was involved, either nasal or laryngeal. Postmortem radiographic studies have failed to demonstrate such obstruction, however.⁷ Marshall found that petechiae were relatively infrequent in cases of plastic bag suffocation and asphyxiation.⁸ Recent interesting work⁶ with rats who were asphyxiated in various ways demonstrated that abrupt tracheal occlusion produced petechiae in only 7 per cent, whereas breathing 100 per cent nitrogen produced petechiae in more than 80 per cent of the animals. Respiratory paralysis with succinylcholine caused petechiae in only 20 per cent, and cardiac arrest with KCl in 27 per cent. The authors conclude that hypoxia, prior to cardiac arrest, and vigorous respiratory movements are necessary to produce intrathoracic petechiae, and that unremitting airway obstruction is unlikely as a cause of SIDS. Instead, they propose that crib death is due to primary apnea, secondary to moderate hypoxia.

In summary, certain infants are predisposed to bouts of cyanosis and prolonged apnea. Although these infants are at risk of dying from SIDS, no one has yet developed a satisfactory method of monitoring them. Prematurity and viral infections seem to be contributing factors. Immaturity or malfunction of central mechanisms of respiratory control may cause apnea as the terminal event.⁵ □

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President's Pages



Dear Fellow Physicians:

Recently, I've had the privilege of visiting the medical societies in Greenville, Orangeburg, Columbia, and the district meeting at Kingstree. Other officers have visited Greenwood and Rock Hill. We have had an excellent reception and feel that we have been better able to bring the current problems to the membership through the individual society meetings. All of your officers and councilors are available for your meetings at your request. We would welcome the opportunity to meet with you and explain the problems and answer the questions that are on your minds.

The Executive Committee had as its guests at the last meeting representatives of the Pharmaceutical Association and we had an excellent dialogue at this session. Physicians' use of the Medicaid drug formulary was encouraged so that some of the problems with specific Medicaid coverage could be avoided at the time the patient's prescription is written. Other suggestions made at this meeting have been referred to various committees for refinement and will be presented to you at a later date.

Again, may I urge all of you to make plans to attend the SCMA House of Delegates meeting and the SOCPAC meeting in Greenville on November 14, 15, and 16. Senator Helms of North Carolina will be the luncheon speaker. We are having a representative from the AMPAC Board with us and representatives from the AMA staff. All resolutions and items of business should be sent to the Headquarters Office from your local societies now so they can be prepared to be referred to the Reference Committees on Saturday afternoon. These committees will make their requests for action to the House of Delegates on Sunday morning, November 16. We urge all of the delegates to make every effort to attend this meeting and also any other members of the local societies who are interested.

Your Executive Committee and that of the S. C. Hospital Association have been meeting together and exchanging ideas and discussing mutual problems. On October 1, Ken Owens, Dessie Gilland, and I attended a meeting with the members of the Hospital Association. Items discussed involved the rural physician recruitment project. We are hopeful of obtaining some funds in the near future to activate our rural health delivery system that we have been working on with Don Kilgore's committee for the last two years. Also, other items discussed have been the proposal of the State Board of Health to require each physician to purchase his prescription blanks in three-copy form. Everyone is opposed to this and your Council and officers are doing everything possible to prevent this from being activated.

We have also had representatives of the Nurses Association meeting with the Council and have discussed in detail the present Nurse Practice Act and the role of the registered nurse in medical care today. You will be hearing more about this in later reports.

Your Council is looking forward to a most productive weekend meeting this month, and we all, Council and county society delegates, look forward to a successful Mid Winter Conference. Join us in Greenville, November 14, 15, and 16.

Sincerely yours,
C. Tucker Weston, M.D.
President



Fifty Years Ago

October 1925

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Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

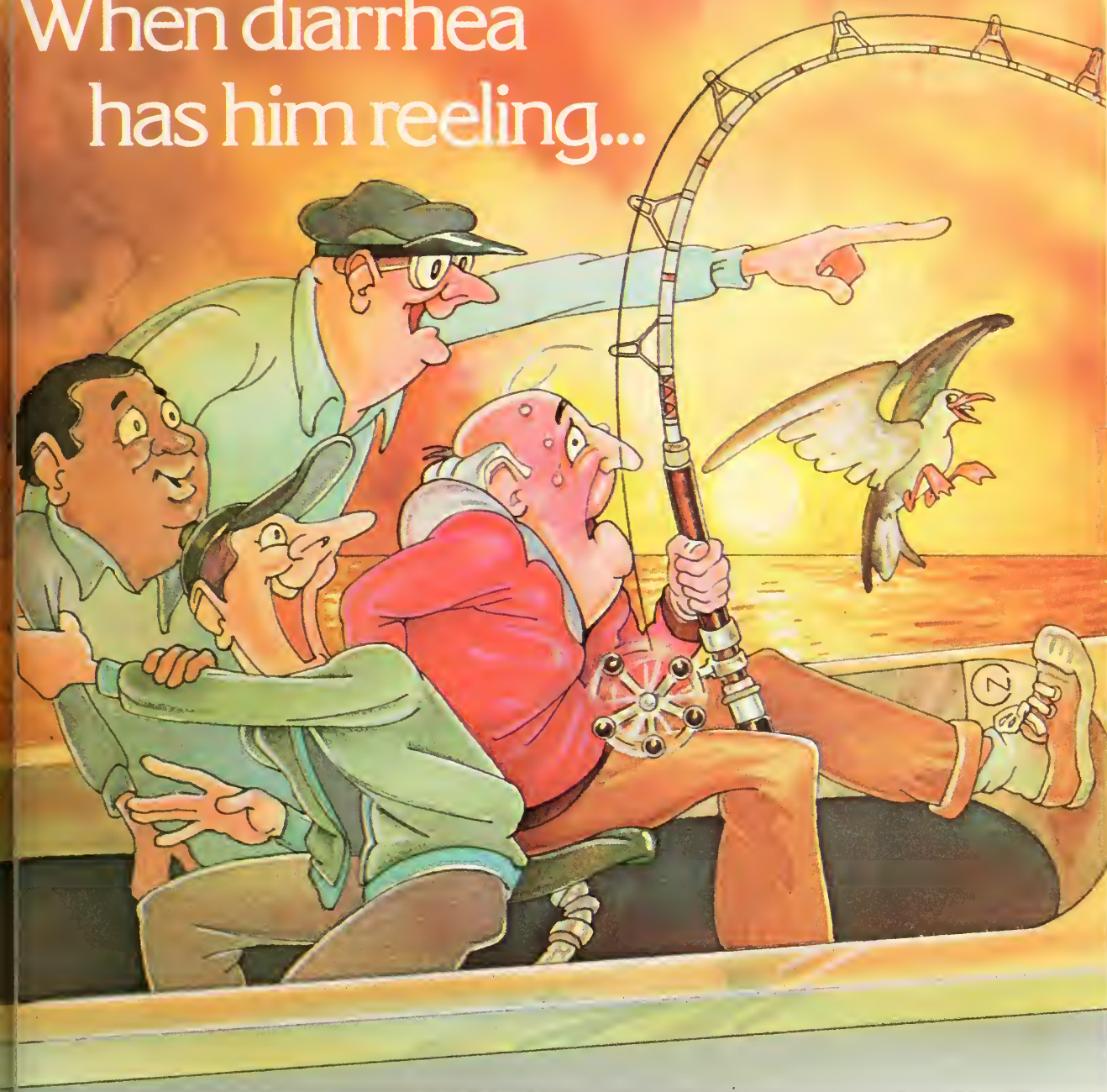
Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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This rapid action can halt the emergency aspect of diarrhea and is comforting and reassuring to the patient. Electrolyte and

fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate specific therapy should be given along with Lomotil.

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Each tablet and each 5 ml of liquid contain: diphenoxylate hydrochloride 2.5 mg (Warning: May be habit forming); atropine sulfate 0.025 mg

In hypertension,

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than effective lowering
of blood pressure...



**With ALDOMET
(Methyldopa, MSD),
existing renal function
is usually unchanged**

ALDOMET has no direct effect on renal function. When used in effective doses, ALDOMET usually does not reduce glomerular filtration rate, renal blood flow, or filtration fraction.



**With ALDOMET
(Methyldopa, MSD),
cardiac output is
generally unchanged**

ALDOMET has no direct effect on cardiac function. When ALDOMET is used in effective doses cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is slowed.



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addendum

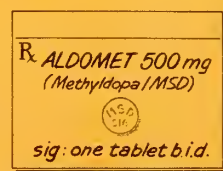
to further
simplify therapy
for many patients

now available
ALDOMET[®] 500 mg
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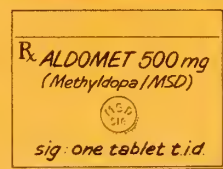
- often more practical to prescribe
- easier for patients to remember

Now offered in addition to the standard 250-mg tablet, the new ALDOMET 500 mg tablet is a patient convenience. An especially important one, since in hypertension convenience of the dosage schedule is one factor that can make the difference in compliance of the patient. The minimum daily dose of ALDOMET is 250 mg b.i.d. The usual starting dose is 250 mg t.i.d. Dosage is adjusted as necessary by adding or deleting 250 mg or 500 mg at intervals of not less than two days. The maximum dose is 3.0 g per day. Examples of b.i.d. or t.i.d. dosage convenience provided by ALDOMET 500 mg within the usual daily dosage range of 500 mg to 2.0 g:

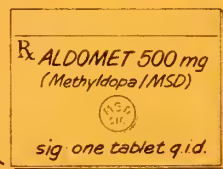
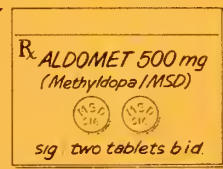
1.0-g
daily
dose =



1.5-g
daily
dose =



2.0-g
daily
dose =



NOTE: Tablets shown are not actual size.

With ALDOMET (Methyldopa, MSD), symptomatic postural hypotension is infrequent

ALDOMET reduces both supine and standing blood pressure. Less frequent symptomatic postural hypotension is experienced with ALDOMET than with many other antihypertensive agents. Exercise hypotension and diurnal blood pressure variations rarely occur.

for hypertension

TABLETS, 250 mg, 500 mg, and 125 mg

ALDOMET[®]

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a unique antihypertensive agent

ALDOMET is contraindicated in active hepatic disease, hypersensitivity to the drug, and if previous methyldopa therapy has been associated with liver disorders. It is not recommended in pheochromocytoma. It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia and liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

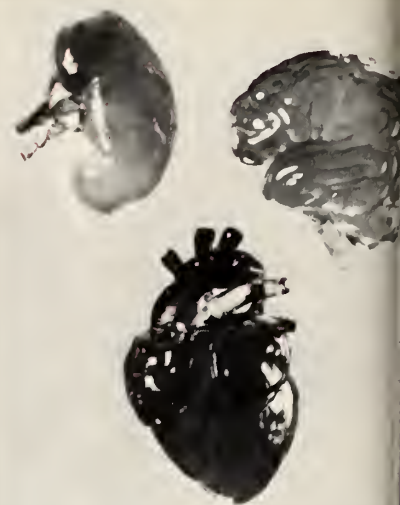
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For a brief summary of prescribing information, please see following page.

in hypertension

ALDOMET[®] (METHYLDOPA/MSD)

usually lowers blood pressure effectively



Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or

cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reaction or unusual manifestations of drug idiosyncrasy.

Use in Pregnancy: Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebral disease. Patients may require reduced anesthetics; hypotension occurring during anesthesia usually can be controlled with vasodilators. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by dialysis.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, early and transient, dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, involuntary choreoathetotic movements; psychic disturbances including nightmares and reversible mild depression.

Cardiovascular: Bradycardia, aggravation of angina pectoris, orthostatic hypotension (decreased dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.)

Gastrointestinal: Nausea, vomiting, constipation, flatulence, diarrhea, mild sore mouth, sore or "black" tongue, pharyngitis, sialadenitis.

Hepatic: Abnormal liver function tests; liver disorders.

Hematologic: Positive Coombs test, anemia, leukopenia, granulocytopenia, thrombocytopenia.

Allergic: Drug-related fever, skin rash.

Other: Nasal stuffiness, rise in BUN, breast engorgement, gynecomastia, lactation, decreased libido, mild arthralgia, myalgia.

Note: Initial adult dosage should be 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur between second and third month of therapy; increased dosage or adding a thiazide restores effective control. Patients with renal function may respond to smaller doses. In older patients may be related to decreased sensitivity and advanced arteriosclerosis; this may be avoided by lower dosage. **How Supplied:** Tablets, containing 250 mg methyldopa each, in bottles of 100; Tablets, containing 500 mg methyldopa each, in packages of 100 and bottles of 100. Tablets, containing 500 mg methyldopa single-unit packages of 100 and bottles of 100. For more detailed information, consult representative or see full prescribing information. Merck Sharp & Dohme, Division Co., Inc., West Point, Pa. 19380

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Kaolin	6.0 g.
Pectin	142.8 mg.
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Non narcotic for 6-8-hr. cough control

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Decongestant action helps control cough and clear stuffy nose and sinuses. Non narcotic.

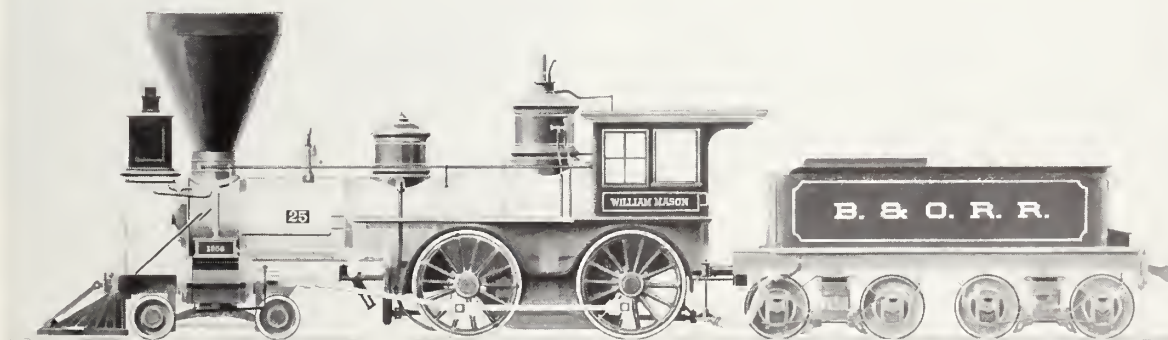
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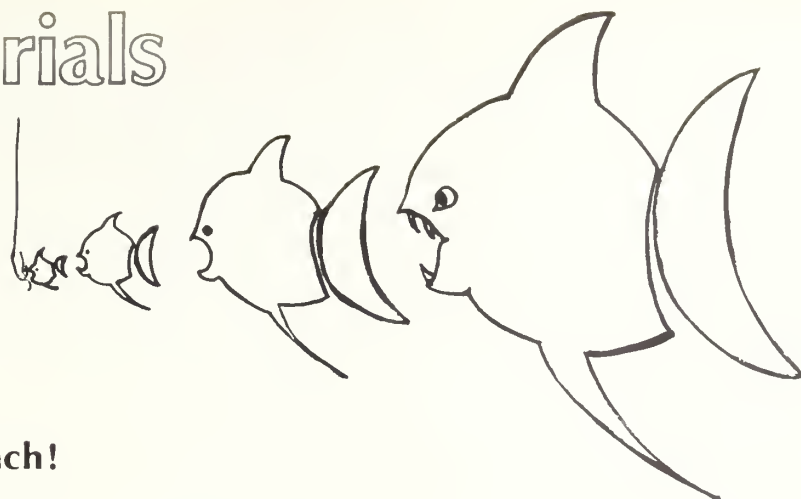


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ACCREDITED BY THE J. C. A. H.

Editorials



No Free Lunch!

A letter in this issue from my good friend and sometimes mentor, Warren Irvin, relates his version of the origin of one of my very favorite bits of philosophy, "There's no such thing as a free lunch." This has been a popular philosophical stance and a truism for a long time. Once there was an international TNSTAAFL Club (the modern cute version would probably be "There's No Such Thing as a Free Lunch Bunch"). But modern events may have invalidated this verity. Consider for a moment that public schools in Richland County District One provided over 2,630,000 free lunches to students during the 1974-75 school year! This is one small area for one year—2.6 million free lunches!! Maybe there now *is* such a thing as a free lunch.

But there are other interpretations! Let's consider the story of Hog Island. Hog Island was in the middle of Great River. It was a wild, rough and tough, craggy island populated only by several scores of wild hogs. These hogs were even tougher than the island and wily to boot. Despite many forays into the island by people from the mainland, never had anyone been able to capture or even kill one of these hogs who dragged their sustenance from the rough, barren surface of Hog Island.

One day, a peasant from the other side of the river began bringing food to the wild hogs of Hog Island. The people who knew about Hog Island thought the man demented. Even though anyone would like to have a few of those hogs in these bad times, everyone knew

the man could not lure those wild, self-sufficient hogs to death or captivity with a few morsels of food. But the man kept it up. Every day he delivered a boatload of food to the same place on Hog Island. At first the hogs completely ignored the food. But one day, one of the old feeble boars tried the easy food, then a sow and her piglet tried it. After a few months, the man found all the food he had brought the day before had disappeared by the time he got there. Not long after, the man found one or two of the hogs waiting in the distance, watching him deliver the food, and then running up to get their feed as soon as the man left the island. Not many more months had passed before the hogs of Hog Island were standing in the clearing waiting for the man every day when he brought the food.

About this time he began building cages for hogs. The people, unfamiliar with the events on Hog Island, thought the man had at last taken complete leave of his senses. He could never get those wild hogs of Hog Island into cages. Those once wild hogs of Hog Island walked into the cages to get their free lunches. The man simply closed the cages and took those well-fed but no longer wild or free hogs across the river and right to the butcher. He kept doing this until there were no more hogs on Hog Island, and now everyone wonders how Hog Island ever got that name.

There is no such thing as a free lunch!!

EEK

Letter to the Editor

Dear Ed:

You have been very kind to publish some of my thoughts in the past and most recently the one on Russia. Yesterday, I asked one of my acquaintances who had helped me with it, had he read it, and he answered by saying, "It's too long." I was reminded of the story about the Shah's advisors being told to abbreviate the 20-volume set of Economics, and after numerous attempts, finally settled with the statement, "There ain't no such thing as a free lunch."

All of this leads up to the fact that I had mentioned to you that I would call to your attention a book by Sir George Pickering entitled *Creative Malady*. Sir George must be a most interesting person and I regret that I have not had the opportunity to know him personally. The book itself is really a "labor of

love" in which he discusses the illnesses, primarily emotional, that were involved in the lives of Charles Darwin (you now see why I bought the book), Florence Nightingale, Mary Baker Eddy, Sigmund Freud, and others. He wrote the book primarily while confined to bed for his arthritic hips which he states were subsequently "totally removed and replaced by metal prostheses. Though it was blissful to be freed from pain and to be no longer crippled, I cannot help regretting the passing of my old friend."

Nevertheless, to be more like the Shah and less like the Russian, I would merely say that I believe all physicians would enjoy the book, both from its content and from Sir George's way of putting things.

With kindest regards,

C. Warren Irvin, M.D.

SCMA Delegates Mid Winter Meeting

More than 100 SCMA members representing 38 county societies will gather in Greenville for the third annual Mid-Winter Conference. The meeting will be held at the Sheraton Motor Inn on Saturday, November 15, and Sunday, November 16. A reception will be held Friday evening, November 14, at 8:30 for early arrivals.

Major topics to be considered at the meeting include legislative proposals for professional liability insurance and reports on the meetings and progress of the S. C. Medical Injury Insurance Reparations Advisory Committee. The latter was established by the General Assembly to study the medical malpractice situation in South Carolina and make recommendations to the legislature.

Most standing committees are expected to meet and make recommendations to the House of Delegates establishing SCMA positions and goals for the second half of the fiscal year. Standing committees will meet from 8:30 to 11:00 Saturday morning and will make recommendations to the House at 3:30 Saturday afternoon. Reference Committees will consider

all recommendations at 5:00 p.m. Saturday for presentation again to the House at 9:00 Sunday morning.

William H. Hunter, M.D., Speaker of the House of Delegates, stated that although the delegates are representing the various county societies and will be the only ones with voting privileges, all SCMA members are invited and encouraged to attend. □

Senator Helms to Address SOCPAC

Senator Jesse Helms (R.-N.C.) will be guest speaker at the workshop of the S. C. Political Action Committee on Saturday, November 15. The SOCPAC meeting which will follow the meetings of Standing Committees will include speakers from AMPAC and the AMA in addition to Senator Helms.

Dr. Kenneth N. Owens of Aiken is Chairman of SOCPAC, a non-partisan group of medical doctors interested in supporting the campaign of politicians believed to best serve the public through their interest and knowledge of the medical profession. All SCMA members are urged to join this committee. □



Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

ould be useful in the management of vertigo* associated with
affecting the vestibular system.

relieve nausea and vomiting often associated with vertigo.*
Adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.
Available as Antivert (meclizine HCl) 12.5 mg. scored
for dosage convenience and flexibility.
Antivert/25 (meclizine HCl) 25 mg. Chewable Tablets for
nausea and vomiting and dizziness associated with motion sickness.

SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS: Based on a review of this drug by the National Academy of
Sciences—National Research Council and/or other information, FDA has classified
indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with
motion sickness.

Probably Effective: Management of vertigo associated with diseases affecting the
vestibular system.

Classification of the less than effective indications requires further
evaluation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during preg-
nancy or to women who may become pregnant is contraindicated in view of the
teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation
has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./
kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate.
Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hyper-
sensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients
should be warned of this possibility and cautioned against driving a car or operating
dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children
have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred
vision have been reported.

More detailed professional information available on
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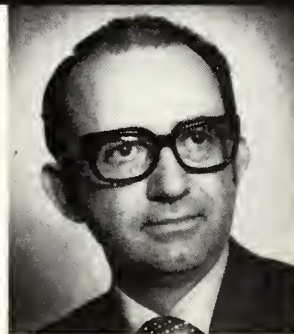
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Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking; some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. This information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages to a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a patient insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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* WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium fre-

quently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy

patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreased alkali reserve with possible metabolic acidosis, hypoglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatic xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Packages of 100 (intended for institutional use only).

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The Consumer Protection Code and Physicians

A Restatement

In the July issue of JSCMA, the types of credit extended by physicians which fall under the S.C. Consumer Protection Code were published. It was stated that if a professional (1) extends credit and collects a service charge, or (2) accepts payment of bills in 4 or more installments, he must register with the S.C. Department of Consumer Affairs.

There has been some question about the practice of physicians accepting (though not formally agreeing to) installment payments and whether or not this acceptance would still put a physician in the position of "extending credit." The Department of Consumer Affairs offers the following for further clarification.

If a physician renders services under an *agreement* with the patient that he may pay the debt in 4 or more installments, he is making a "consumer credit sale," whether or not any charge is made in connection therewith:

If a physician renders services under an arrangement which gives the patient a right to pay the debt at some agreed future time along with a *credit service charge*, he is making a "consumer credit sale," whether or not the debt is payable in installments:

If a physician renders services under a billing arrangement which gives no right to defer payment but which requires prompt payment in full, he is not making a consumer credit sale even though he makes an *interest charge on past due balances*.

(*Agreement* means the bargain of the parties in fact as found in their language or by implication from other circumstances including course of dealing or usage of trade or course of performance.

(*Credit service charge* is that charge made as an incident to the extension of credit.

(*Interest charge on past due balances* is a charge for forbearance of a debt, no credit is involved.)

It is hoped that the terms and definitions listed above will help physicians determine

their obligations under the Consumer Protection Code. If a physician finds that his office procedures would indeed qualify him as "extending credit," he should contact the S.C. Department of Consumer Affairs, P.O. Box 11739, Columbia SC 29211, tel. 758-2040, for registration procedures. □

Some Unexpected Results of M.D.'s Demands for Malpractice Legislation

An editorial in the August 1975 issue of the Federation Bulletin, published by the Federation of State Medical Boards, has called attention to some disturbing and generally unknown results of new malpractice legislation in two states.

Parts of the malpractice legislative reform packages in New York and California indicate that when physicians demand legislative reform, they sometimes get more than they bargained for.

In California, according to the Federation editorial, "The legislature is proposing to correct physician maldistribution and to impose tighter controls on medical practice as a part of the package. It is also possible that the majority of the California examining board will be non-physicians on the theory that doctors protect themselves rather than the public."

In New York, a new law has been adopted. In it: "discipline of physicians has been moved from the Board of Medicine to the Department of Health. The change was made, according to the state government, because the medical board has been too slow and too lenient in dealing with problem doctors."

In South Carolina, physicians should take note of this trend on the part of legislative bodies to use the malpractice crisis as an opportunity to extend the state's control over the practice of medicine. □

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□

PSRO Progress Report

On September 1, 1975, PSRO review of Medicare and Medicaid patients was initiated in the following hospitals: Richland Memorial, Providence, Lexington County, Hilton Head, Spartanburg General, and B. J. Workman Memorial.

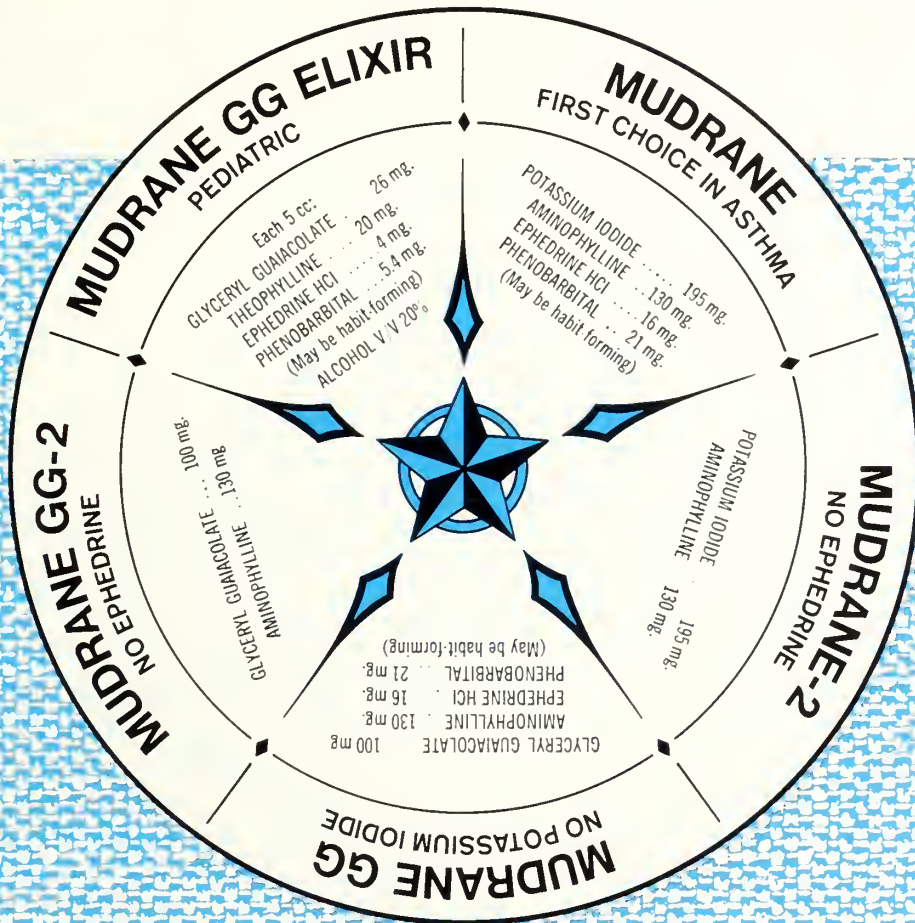
The next group of hospitals will be implementing PSRO review on November 3, 1975. These hospitals include Orangeburg General, Hampton General, Marlboro County, Allendale County, Medical University of South Carolina, Jasper County, Wilson Clinic, Elliot White Springs Memorial Hospital, Aiken County, and Lee County.

Membership in the Medical Care Foundation continues to grow with over 1800, or 70%, of the South Carolina physicians on file as members.

□

The MUDRANES

Discreet formulations of four well regarded drugs for the relief of bronchial distress—Potassium Iodide, Glyceryl Guaiacolate, Aminophylline, Ephedrine with Phenobarbital (to lessen cardiac stimulation).



INDICATIONS: For the prompt symptomatic relief of bronchial asthma, emphysema and bronchiectasis. The Mudranes dilate the bronchi and liquefy mucus plugs. **DOSAGE:** Tablet; One tablet with a full glass of water 3 or 4 times daily as required. Divide tablet for child's dose. Elixir; Children, 1 cc for each 10 lbs. of body weight. May be repeated 3 or 4 times a day. Adult, one tablespoonful 4 times daily. All doses should be followed with a glass of water.

CONTRAINDICATIONS: Aminophylline/Theophylline is contraindicated in the presence of severe cardiac arrhythmias and patients with massive myocardial damage. Ephedrine, in presence of severe heart disease, extreme hypertension, and in hyperthyroidism. Phenobarbital, in porphyria and in patients with known phenobarbital sensitivity. Potassium Iodide, in pregnancy (to protect the fetus against possible iodine-induced depression of thyroid activity), in tuberculosis (produces gumma dissolution), and in acne; also in the presence of known iodide sensitivity. **PRECAUTIONS:** Aminophylline/Theophylline should be avoided in patients with massive myocardial damage and/or severe cardiac

arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdose. Potassium Iodide: Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing anginal pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdose. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

HOW SUPPLIED: Mudrane and Mudrane GG available in bottles of 100 and 1000 tablets; Mudrane-2 and Mudrane GG-2 in 100s; Elixir in pints and half-gallons.

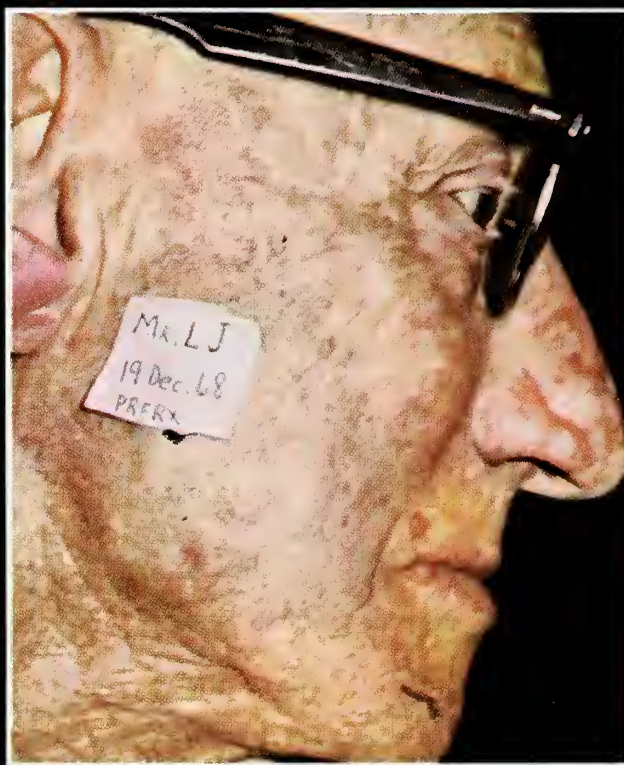
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the sun and solar keratosis...

Over- exposed



and often underdiagnosed

Solar keratosis is not an uncommon medical problem.

Of course, the prevalence of keratotic lesions is greater in locations south of the 38th parallel—the so-called "Solar Keratosis Belt"—receiving the greatest amounts of solar radiation. However, solar keratosis can occur among any light-skinned population, usually in persons over 40, wherever people are subject to extended exposure to the sun.

Solar keratoses are generally not difficult to identify.

These skin lesions are usually multiple, flat or slightly elevated, brownish or red in color, papular, dry, rough, adherent and sharply defined. They are found on areas of the skin having extensive exposure to sunlight. Clinical characteristics of the lesions, their predominant location on exposed surfaces, the age of the patient and his skin type are important considerations in the diagnosis.

Solar keratoses can, and should, be treated because they are potentially premalignant.

Chronic exposure to sunlight frequently leads to degenerative changes in the skin. This can often result in the development of multiple, potentially premalignant keratotic lesions. Therefore, early detection and treatment is advisable.

Treatment with Efudex (fluorouracil) provides a high degree of effectiveness with a low recurrence rate, ease and convenience of therapy, low incidence of scarring, excellent cosmetic results in most cases, and a high level of patient acceptability.

Efudex® 5% Cream fluorouracil/Roche®

Because there may be more than meets the eye.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may cause inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to

respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulocytosis and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dis-

pensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris (hydroxymethyl) aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



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Nutley, New Jersey 07110

See history for patient photographed at left on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



WOMAN'S AUXILIARY TO THE SOUTH CAROLINA MEDICAL ASSOCIATION

As we move into the work of the Auxiliary for the year we welcome the opportunity to share with you some of the Auxiliary activities.

The Fall Board meeting of the South Carolina Medical Auxiliary will be held on October 30 at 10:30 a. m. at the Sheraton Inn in Spartanburg. We look forward to having Dr. Tucker Weston as the luncheon speaker. May I take this opportunity to express to the Advisory Council to the Auxiliary from the South Carolina Medical Association our appreciation for your guidance and support. The Advisors for the year are Dr. C. Tucker Weston, Dr. John M. Shingler, Jr., Dr. Wayne Brady, Dr. Lucius Cline, Jr., and Mr. Charles Johnson.

A special congratulations to the Charleston County Auxiliary on the celebration of its 50th Anniversary for fifty years of leadership in Auxiliary affairs. We appreciate your years of service.

The State President and President-Elect of the Auxiliary along with four County Presidents-Elect will be attending a Leadership Conference in Chicago on October 13-15. The County Presidents-Elect attending will be: Mrs. Joseph Nannerello of Greenville, Mrs. Hubert Bowick of Pickens, Mrs. Karl V. Doskocil of Columbia, and Mrs. Ronald Lanford of

Spartanburg. It is the hope of the AMA Auxiliary that the Leadership training for County Presidents-Elect will help them to work more effectively during their terms of office as President.

In October the South Carolina Medical Auxiliary will be involved in the Immunization Action Month. The State Auxiliary representative to this project is Mrs. Alton Brown of Rock Hill, Auxiliary Community Health Chairman.

Mrs. Brown and the Community Health Chairman from each county will again this year assist the South Carolina Chapter of the American Academy of Pediatrics in sponsoring a poster contest on Poison Control and Accidental Poisoning in Children.

Many county auxiliaries have a Christmas Card Project to raise funds for AMAERF. This is an excellent way to make money for this most worthwhile endeavor. We urge your consideration and support. The County Auxiliary sends a Christmas card to each physician family in the County in the name of all of the contributors to the AMAERF Christmas Card Project who are listed thereon.

SARA SHINGLER

Famous Fighters



JOHN L. SULLIVAN
Bare-knuckles heavyweight champion
1882-1892

NEOSPORIN® Ointment (polymyxin B-bacitracin-neomycin) is a famous fighter, too.

Provides overlapping, broad-spectrum antibacterial action to help combat infection caused by common susceptible pathogens (including staph and strep).

Each gram contains Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

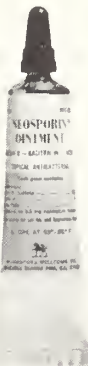
INDICATIONS: Therapeutically (as an adjunct to systemic therapy when indicated) for topical infections, primary or secondary, due to susceptible organisms, as in:

- infected burns, skin grafts, surgical incisions, otitis externa
- primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia)
- secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis)
- traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to



neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

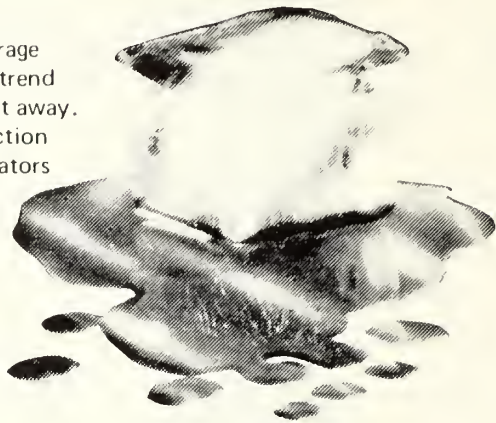
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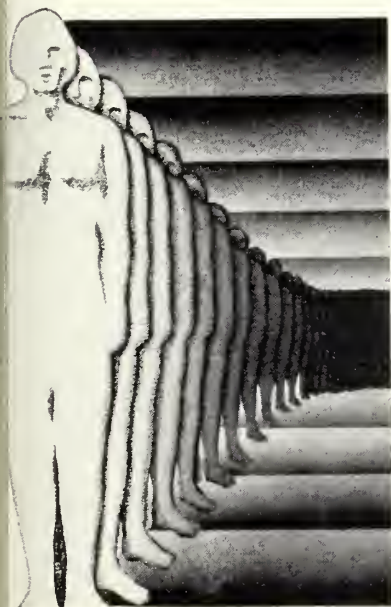
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PERFORMANCE. IT'S A MATTER OF RECORD.

- an unsurpassed record validated in several thousand clinical papers
- rarely interferes with mental acuity
- wide margin of safety



Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous

occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. *Oral—Adults:* Mild and moderate anxiety and tension, 5 to 10 mg *t.i.d.* or *q.i.d.*; severe states, 20 or 25 mg *t.i.d.* or *q.i.d.* *Geriatric patients:* 5 mg *b.i.d.* to *q.i.d.* (See Precautions.)

Supplied: Librium® (chlordiazepoxide HCl) Capsules, 5 mg, 10 mg and 25 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Libritabs® (chlordiazepoxide) Tablets, 5 mg, 10 mg and 25 mg—bottles of 100 and 500. With respect to clinical activity, capsules and tablets are indistinguishable.

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LIBRIUM®

chlordiazepoxide HCl/Roche
5mg, 10mg, 25mg capsules

**IN PAINFUL
ACUTE
CYSTITIS***

*nonobstructed;
due to susceptible
organisms



RELIEVE THE PAIN WHILE YOU ELIMINATE THE PATHOGENS.

FOR THE PAIN

- ☐ **Early relief of painful symptoms** such as burning and pain associated with urgency and frequency.

FOR THE PATHOGENS

- ☐ **Effective control of susceptible pathogens** such as *E. coli*, *Klebsiella-Aerobacter*, *Staph. au-*

reus, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

Appropriate antibacterial therapy: Up to 3 days therapy with Azo Gantrisin 4 to 6 tablets *Stat.*, then 2 tablets *q.i.d.*; then 11 days with Gantrisin (sulfisoxazole) may be considered.

AZO GANTRISIN®

(50 mg phenazopyridine HCl and 0.5 Gm sulfisoxazole)

Before prescribing, please consult complete product information, a summary of which follows.

Indications: In adults, urinary tract infections complicated by pain (primarily cystitis, pyelitis and pyelonephritis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies.

Important Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents including the sulfonamides. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period. Contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.

Warnings: Safe use in pregnancy has not been established. Teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* Agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia.

Allergic reactions: Erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis. *C.N.S. reactions:* Headache, periph-

eral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Usual adult dosage for acute, painful phase of urinary tract infections is 4 to 6 tablets initially, then 2 tablets four times daily for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment of the infection with Gantrisin (sulfisoxazole) may be considered.

Note: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine soon after ingestion.

How Supplied: Tablets, each containing 0.5 Gm sulfisoxazole and 50 mg phenazopyridine HCl—bottles of 100 and 500.

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Both often



Predominant
psychoneurotic
anxiety

Associated
depressive
symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor

neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuation (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent

in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

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Valium® (diazepam) [Ⓢ]IV

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

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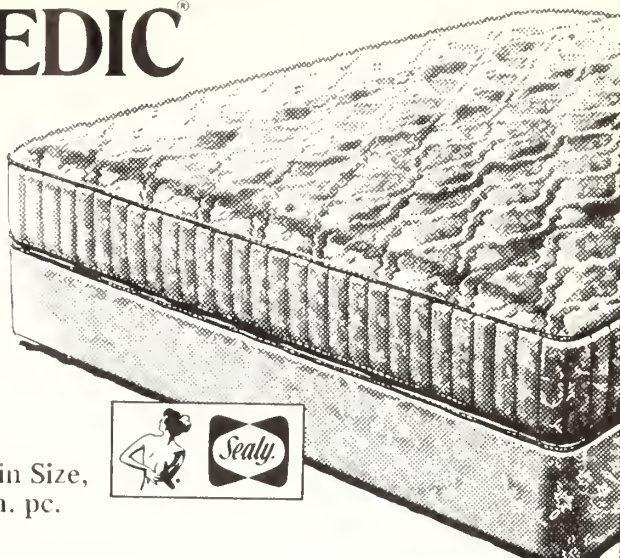
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POLYMYALGIA RHEUMATICA

C. WALLACE HARPER, M.D.*

Polymyalgia rheumatica is a self-limiting syndrome of proximal muscular discomfort and stiffness occurring almost exclusively in the older patient. It is usually accompanied by other systemic manifestations and characterized by a striking elevation of the sedimentation rate and by dramatic symptomatic response to minimal doses of corticosteroids.^{1, 7, 9, 12, 28, 29, 32}

It is an important syndrome for a variety of reasons. One of these is the fact that it is more common than has been realized.^{1, 12, 21} Secondly, it has been considered a clinical entity in this country for only a little more than a decade. The first paper on the subject appeared in the American literature as recently as 1963. Until recently, standard textbooks have paid little attention to the problem; consequently, many physicians remain unfamiliar with the condition and the diagnosis is commonly overlooked or delayed.^{7, 12, 17}

As more and more elderly patients are being seen, the potential for making this diagnosis increases and physicians should familiarize themselves with polymyalgia rheumatica and its associations, since in most instances it is a completely treatable rheumatic condition.

The most valid reason for the importance of this syndrome, however, is the significant role it plays in the clinical spectrum of giant cell arteritis. Many feel that it is always associated with the latter. Others, though apparently in the minority, disagree, feeling that other conditions may cause polymyalgia rheumatica although agreeing that systemic giant cell arteritis is the most frequent underlying cause.⁹ In any event, the association is frequent enough so that the finding of polymyalgia rheumatica should be regarded as a clue to the presence of systemic giant cell arteritis.^{1, 12, 17} This is of practical significance because of the varied complications that may occur with giant cell arteritis which, though usually not fatal, are disabling and may on occasion pose a threat to survival. The most feared complication, however, is that of the development of sudden and irreversible loss of vision. The risk of blindness in polymyalgia rheumatica without clinical or histological evidence of giant cell arteritis is low, but, nevertheless, is felt to be a hazard.^{9, 32}

The incidence of polymyalgia rheumatica is unknown. While rare among the general population, it is not uncommon among the aged, being more common in the seventh or eighth decades, with an average age ranging from 65 to 70.^{7, 16, 17, 21} Although it may, it un-

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commonly affects those under age 55.²⁹ It affects females twice as commonly as males.¹⁷ Dixon, et al, found it about half as common as rheumatoid arthritis when the comparison was limited to age 70 or above, and irrespective of age, they found its incidence greater than ankylosing spondylitis and about equal to that of gout.²¹

The condition is self-limiting, but lasts on an average of two to three years with a range of six months to six years.¹⁷ The duration may be greater, however, and one case is on record of having persisted for fourteen years.²⁸ Activity may be episodic in nature, characterized by remissions and exacerbations, but once the disease has run its course, recurrence is thought to be rare.¹²

The clinical picture is that of proximal muscle aching and stiffness. The muscles of the pectoral and pelvic girdles are usually affected with involvement of the muscles distal to the elbows and knees being unusual. Discomfort is usually bilateral and frequently symmetrical. Pain on motion and early morning stiffness, improving with activity, are prominent features. Some, however, feel that nocturnal pain is not uncommon. The onset of myalgias may be insidious or abrupt with the patient remembering the exact time of initial involvement. Most patients complain of discomfort in the area of the shoulders, neck, back, buttocks, or thighs. In advanced cases, even slight movement has been described as causing severe, stabbing pain followed by residual aching with resultant limitation of motion. The degree of involvement may be mild, moderate, or severe to the point of incapacitation.^{7, 12, 17, 18} Arthralgias are not a feature of the PMR syndrome, but periarticular involvement occasionally occurs. Transient swelling may occasionally affect any joint with knee effusions occurring more commonly.^{7, 17} Tenderness of tendons or tendinous insertions sometimes occurs and sternoclavicular tenderness and swelling have been reported.²⁷ Active joint movement is often prohibited by pain and capsulitis of the shoulder leading to a frozen joint is a possibility if prompt treatment is withheld.⁷ Marked inflammatory synovitis and joint destruction are not present.¹

Systemic manifestations often accompany the myalgic picture and include malaise, apathy, fatigue, anorexia with weight loss,

anemia, fever and headache due to temporal arteritis. Overt evidence of giant cell arteritis involving other vessels may occur. Psychological symptoms are common and include depression, mental deterioration, and rarely the development of psychosis.^{1, 7, 9, 12, 13, 17, 28}

The outstanding laboratory feature of polymyalgia rheumatica is the presence of a strikingly elevated ESR. This is an important diagnostic aid since it is usually above 70 mm. and almost never below 50mm./hour. Frequently, it is above 100 mm./hour if the Westergren method is used. The degree of elevation is thought to parallel the level of activity of the condition, hence affording an important aid in evaluating the therapeutic response to treatment.^{4, 9, 12}

Plasma proteins are altered with common findings limited to an elevation of alpha-2 globulins, elevated fibrinogen levels and diminished serum albumin.^{4, 9, 12}

A mild hypochromic or normochromic normocytic anemia is common. The serum iron may be decreased with a normal ironbinding capacity, but marrow studies have shown normal marrow iron to be present. Erythroid maturation is also normal.^{17, 23}

Other laboratory studies frequently done in rheumatic diseases are normal and useful only insofar as they help to exclude other conditions. Among these are tests for rheumatoid factor, LE cell preps, antinuclear-antibody test, serum enzyme studies, electromyography and muscle biopsy.^{1, 9, 17, 32}

Historically, polymyalgia rheumatica was first described in 1888 by Bruce, a Scottish physician. He described five cases which he termed "senile rheumatic gout." These were elderly individuals who spontaneously recovered after one to two years. The author noted the condition was remarkable for its severity and complete curability.³¹

Little attention was paid this condition for decades with sporadic reports occurring in the European literature under a variety of names; however, reports have been frequent in the European literature for the past thirty to forty years.

In 1932, giant cell arteritis was first described as temporal arteritis.³³ Subsequently, it has been shown that in giant cell arteritis there is widespread arterial involvement of large and medium sized vessels.^{4, 16, 22, 30} In

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1956, Pauley, noting the frequency of polymyalgia rheumatica symptom in the prodromal phase of temporal arteritis, postulated that this was really temporal arteritis in one of its guises.^{30, 13} This suspicion was confirmed in 1963 by Alestig and Barr who demonstrated temporal arteritis by biopsy in patients with polymyalgia rheumatica without clinical evidence of temporal arteritis.³ The association of polymyalgia rheumatica with temporal arteritis and other forms of giant cell arteritis is now well known.^{1, 2, 4, 9, 12, 14, 16, 17, 18, 22, 28, 29, 32}

The etiology of giant cell arteritis remains an enigma but there has been speculation that it is related to an auto-immune process.^{8, 29, 30} and there is some recent supportive evidence for this concept. Liang, et al, using immunoglobulins and complement within the temporal artery wall in several patients with temporal arteritis, and believed that this resulted from phagocytosis of antibodies complexed with antigen and complement within the vessel wall. They postulated that elastin is antigenic, thus attracting antibodies and that the resulting complex attracts phagocytes with subsequent release of lysozyme, causing further disruption and degeneration of elastic tissue.¹⁰ The electron microscopy studies of Reinecke and Kuwabara, however, suggested that smooth muscle cells in the media and not elastic tissue are the victims of an auto-immune process. They felt the degeneration of smooth muscle cells occurs first and that fragmentation of elastic fibers and giant cell reaction are secondary to this.⁸

Histologically, giant cell arteritis is a panarteritis with prominent cellular infiltration being most marked in the media adjacent to the internal elastic lamina. Lymphocytes and mononuclear cells predominate early with multinuclear giant cells being seen later. The latter are by no means a constant feature, however. There is patchy necrosis of the media with destruction and fragmentation of the internal elastic lamina. Fibrosis of the intima and adventitia occur and fibrous swelling of the intima leads to lumen encroachment and/or occlusion.³⁰ This process is patchy and involves the vessel focally in longitudinal fashion so that involved areas may be adjacent to areas with normal architecture.²⁸ Corticosteroids in

adequate doses usually suppress and may reverse the inflammatory process,^{6, 12, 14, 17, 24, 26, 28, 29, 30, 31} but they are not believed to shorten the course of the arteritic process.¹⁷

Giant cell arteritis involves the arterial tree in centripetal fashion from the aorta and its great vessels down through the medium sized arteries with the smaller arterial vessels being spared.^{16, 22, 18, 29} For practical purposes, it can be said that any artery large enough to have a specific name may be involved and thus giant cell arteritis can emerge in a variety of clinical ways which may include transient cerebral ischemia, cerebral vascular accidents, aortic dissection, aortic arch syndrome, myocardial insufficiency and/or infarction, mesenteric artery involvement, vascular insufficiency of the extremities, etc.^{5, 6, 28, 29} Conspicuously, the pulmonary and renal vessels are usually spared.²⁹

Temporal arteritis seems to be the most frequent clinically detectable presentation of giant cell arteritis and this is fortunate because it is present in most patients who develop visual problems.²⁶ The frequency of visual loss in association with temporal arteritis approaches fifty percent.²⁴ Hence, the presence of temporal arteritis clinically, or proven by temporal artery biopsy, alerts the physician that the patient is at great risk for loss of vision. For this reason, it is imperative that the physician be familiar with the clinical picture of temporal arteritis.

Temporal arteritis is characterized most often by headache which is classically temporal in location but may localize in the orbital, peri-orbital or occipital areas. It may be unilateral or bilateral.¹⁹ Not infrequently, intermittent claudication on chewing due to arterial insufficiency of the masseter muscle has been described.^{28, 35} Other features have been temporal scalp tenderness, excessive sweating in the temporal area,^{26, 28} and diminished sensation to taste and smell.⁵ Physical signs may include a tender temporal artery with diminished to absent pulsations; however, none of these signs may be present and it is well known that active temporal arteritis may exist with the patient being completely asymptomatic. Rarely, ischemic necrosis of the temporal scalp²⁶ or anterior tongue have occurred.²⁹

Visual disturbances are common in as-

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sociation with temporal arteritis and are indicative of involvement of the ophthalmic or central retinal arteries.^{24, 26} Problems arise because, infrequently, blindness may be the initial manifestation of giant cell arteritis,^{2, 9, 12, 24, 25, 26} and, as mentioned above, temporal arteritis may be present histologically and yet be clinically silent.^{9, 12, 24, 15, 28} The development of any visual disturbance in a patient who has temporal arteritis, with the PMR syndrome, or who is suspected of having giant cell arteritis is a grave prognostic sign carrying the risk of permanent visual loss of the affected eye. The patient may complain of blurred vision, transient visual loss, scotomata, photophobia, diplopia, and may on occasion exhibit transient extraocular palsy with the third and sixth cranial nerves most commonly involved.^{24, 26, 28, 29} In Russell's series, the common visual complaint was blurred vision involving part or all of the visual field, progressing to blindness over the next twelve to twenty-four hours, or more gradually over several days.²⁶

Visual loss is due to decreased blood supply to the optic nerve and/or retina. The eyes may be affected in three ways. Most commonly, this occurs as a result of ischemic optic neuritis which may lead to partial or complete loss of vision in the affected eye. Funduscopic examination may reveal a pale, swollen disc with ischemic patches and/or hemorrhages in the adjacent retina. With retrobulbar ischemic neuritis, blindness occurs without observable change in the disc or retina. The third manner in which visual impairment is brought about is by occlusion of the central retinal artery producing retinal ischemia reflected by a pale ischemic retina with edema and development of a cherry-red spot in the macular area.²⁴

The diagnosis of polymyalgia rheumatica is one of exclusion. Conditions which often mimic this syndrome are connective tissue disorders, occult malignancies and latent infections. There is usually no problem with diagnosis since these conditions in time present features that make the underlying problem apparent.¹ Diagnosis is made easier by being knowledgeable about this syndrome and its presentations. This, plus a high index of suspicion, especially when the patients are elderly, allows one to screen appropriately

with sedimentation rates and should readily enhance arriving at the diagnosis. If polymyalgia rheumatica is suspected, a temporal artery biopsy probably should be done early in the diagnostic evaluation rather than delaying this until the last resort as is commonly done.² If positive, it confirms the diagnosis and identifies the patient at great risk of visual complications.^{2, 17} This information is valuable therapeutically, since larger doses of steroids are required in the presence of temporal arteritis.¹⁷ It is important, however, to realize that a negative biopsy does not exclude the diagnosis of temporal arteritis.

Administration of small doses of corticosteroids may be helpful in the diagnosis of polymyalgia rheumatica. Prednisone in amounts as small as ten to twenty milligrams daily may have dramatic results, with disappearance of myalgic and other systemic symptoms in a matter of hours.^{1, 17} It is felt that no other condition is likely to exhibit as striking a response to this dosage.²⁸ Larger doses of steroids are not given on the presumption that they would dilute the specificity of this response.²⁹

Steroid therapy is specific therapy in polymyalgia rheumatica and most feel that corticosteroids should be used in face of inherent risks even in the aged because of the alternative risks of complications and symptomatic discomfort.^{1, 2, 5, 7, 9, 12, 17, 24, 26, 28} A small minority have recommended various analgesics in preference to steroids in cases where there is no evidence of overt arteritis.^{19, 20} While these preparations may afford some symptomatic relief, their use is hazardous since they do not influence the underlying arteritis and may actually mask it, creating a false sense of security.¹⁵ Furthermore, salicylates, indomethacin, and phenylbutazone have dangerous side effects in their own right, especially in the elderly.

While small doses of steroids may give symptomatic relief in polymyalgia rheumatica, it is important to recognize that larger doses are necessary for treatment of active arteritis. For this reason, many authors, feeling that the PMR syndrome is almost always a manifestation of underlying systemic giant cell arteritis, believe that large doses of steroids should be given initially in all cases with subsequent gradual dosage reduction.^{1, 2, 12, 21} Others, in view of the dangers with their use in the elderly, do not feel that large doses of corticosteroids

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are justified unless the patient is in a high risk situation with evidence of temporal arteritis, visual disturbance, or has other overt signs of giant cell arteritis.¹⁷

Steroid therapy should encompass the goals of:

1. Symptomatic relief until the disease has run its course.
2. Prevention of serious complications of arteritis by suppression of activity as measured by symptomatic response and manifested by a normal ESR.
3. The use of the lowest possible dose of steroids to achieve the first two goals.²⁸

The therapeutic regimen proposed by Fernandez-Herlihy appears logical.¹⁷ In this regimen, the author feels that temporal artery biopsy is optional; whereas, many authors^{2, 17} emphasize the importance of performing this procedure, especially in the patient who has the so-called pure polymyalgia rheumatica syndrome without evidence of temporal arteritis. It is well known that temporal arteritis may exist asymptotically²⁵ and a temporal artery biopsy, if positive, identifies the fact that the patient has considerable risk for loss of vision.^{17, 28}

A logical plan of management would seem to be a slight modification of this regimen as follows:

1. Careful examination to exclude other conditions that may mimic polymyalgia rheumatica.
2. Perform temporal artery biopsy early in the course of a work-up. If negative, as many are in the presence of temporal arteritis, consider repeating the biopsy on the opposite temporal artery, especially if clinical suspicion is high. This is a simple office procedure without risk. Make sure the surgeon chooses a biopsy site appropriately and obtains an adequate specimen. The latter should be at least 1 cm. in length and preferably 2 cm. if possible. Request that the pathologist obtain serial sections of the specimen. The arteritic process is known to involve the vessel focally with numerous skipped areas, thus a random section may be normal.
3. If temporal artery biopsy is negative and there is no clinical evidence of temporal arteritis, overt giant cell arteritis else-

where, or visual disturbance, then proceed with treatment with 15 to 20 milligrams of Prednisone daily, given preferably each morning in a single dose. If symptoms subside promptly, followed by a fall in the ESR to normal in a week or two, then continue in this maintenance dosage with gradual attempts to taper to the lowest effective dose. Attempts to lower dosage should be made every two months with careful monitoring. An immediate increase in dosage will be required with any clinical exacerbation or rise in the erythrocyte sedimentation rate. This is especially important if there is any occurrence of visual disturbance.

4. If the temporal artery biopsy is positive, if the patient has clinical evidence of temporal arteritis, other evidence of overt arteritis, or, most importantly, has any visual problems, the initial dose of Prednisone should be 40 to 60 milligrams daily for two to three weeks, or perhaps longer, with gradual reduction to an effective maintenance dose as previously outlined above.

All patients should be fully informed about their condition and its possible complications, with particular emphasis on the signs and symptoms of temporal arteritis, or the development of any visual disturbance which requires immediate physician contact and prompt institution of adequate steroid therapy.^{28, 29}

Periodic physician follow-up is mandatory with regular monitoring of the sedimentation rate advised. It is important for both patient and physician to realize that polymyalgia rheumatica may require several years to run its course and that there may be episodic periods of symptomatic improvement while the underlying arteritis smolders quiescently, thus creating the necessity for low-dose steroid therapy over a period of several months to several years.

In summary, it appears that the polymyalgia rheumatica syndrome is a likely manifestation of giant cell arteritis and should be considered a clue of its presence. Furthermore, it may occur several weeks to a year, or even longer, in advance of other manifestations of underlying arteritis.^{9, 12, 18}

The real significance of polymyalgia rheumatica is that it harbors the threat of permanent loss of vision² which has been estimated

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to occur in 2-1/2 percent of patients without other clinical evidence of giant cell arteritis.⁹ When associated with temporal arteritis, this risk escalates to fifty percent and this association is believed to occur in fifty percent of cases of polymyalgia rheumatica.⁹ The evidence is clear that cranial arteritis may be asymptomatic and that blindness may occur suddenly without prior symptoms.^{2, 25} Fortunately, however, warning signals are present

in most instances, and visual catastrophe can be averted with appropriate corticosteroid therapy.

The diagnosis of polymyalgia rheumatica is one that should not be missed or delayed, and familiarity with this syndrome and its ramifications, in most instances, presents the alert physician with a real therapeutic opportunity. □

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Ragan, C.: The Clinical Picture of Rheumatoid
Arthritis in Arthritis, ed. 8, edited by J. L.
Hollander and D. J. McCarty, Jr., Philadelphia,
Lea & Febiger, 1972, chap. 21, p. 335.

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Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of fever, sore throat, oral lesions (symptoms of blood dyscrasia), dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications: Children 14 years or less, senile patients, history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy, blood dyscrasias, renal, hepatic or cardiac dysfunction, hypertension, thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonyleurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmologic examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals. Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug, its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

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MANAGEMENT OF CANCER OF THE LARYNX

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Cancer of the larynx is an excellent example of a malignancy where early diagnosis, radiotherapy, surgery, and chemotherapy have been making remarkable gains in respect to cure. In certain cases, a combination of treatments appears to be the optimum approach, although the maximum potential of these combinations has still to be achieved. It is even more satisfying that cure, in many instances, is now accompanied by an almost perfect functional result and that rehabilitation is easing the burden on others.

For this discussion, the larynx is divided into three major anatomic sites: the supraglottis, glottis, and subglottis.

INCIDENCE AND ETIOLOGY

Laryngeal cancer represents about 1 per cent of all malignancies with a 10 to 1 predominance in males. The typical male patient who develops cancer of the larynx will usually be in the lower socio-economic group, a heavy smoker, and frequently a moderate to heavy whiskey drinker. The average age is sixty.

Considering the various sites, glottic lesions predominate occurring 70 per cent of cases, with supraglottic 25 per cent, and subglottic the least.

ANATOMY

There is a clear definition of the three regions of the larynx. Each is related to presentation, symptoms, spread by lymphatics and, therefore, therapeutic approach.

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The three regions are: Figure 1.

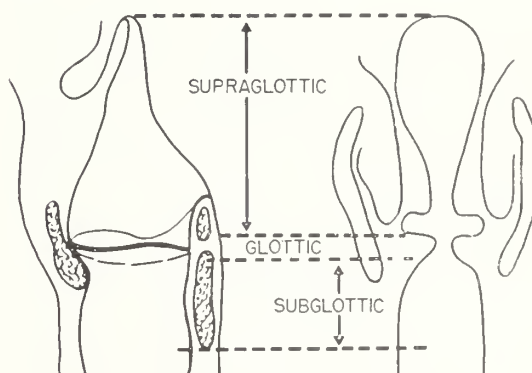
A. Supraglottic Region

The supraglottic region includes the laryngeal surface of the epiglottis, aryepiglottic fold, arytenoids, false cords and ventricular cavity.

Lymphatics are plentiful through this region with the exception of the tip of the epiglottis. The lymphatics pass through the thyrohyoid membrane to the lymph nodes of the upper internal jugular chain. Where these lymphatics traverse the pre-epiglottic space, they communicate freely with one another and drainage may occur bilaterally.

B. Glottis

The glottic region consists only of the true vocal cords and anterior commissure. The lymphatic drainage of the glottis is extremely sparse with eventual drainage into the upper internal jugular chain.



Anatomic Subdivisions of the Larynx

Fig. 1

C. Subglottic Region

The subglottic region excluding the under surface of the true vocal cord extends to the lower margin of the cricoid cartilage. Lymphatics are not very plentiful in this region either. Drainage is to a pretracheal node, nodes in the mid and lower internal jugular chain and the thyroid gland.

CLINICAL ASSESSMENT AND STAGING

By far the most common presenting symptom is hoarseness, intermittent initially, but finally persistent. Dysphagia is a late symptom usually signifying extension of disease to pharynx. Sometimes, dysphagia and a "sticky" pain will precede hoarseness in lesions of the supraglottis. Pain is a very late symptom. A metastatic lymph node is an unusual primary presentation for laryngeal cancer.

Any patient with hoarseness should have an adequate laryngeal examination. A mirror view should suffice, but if not adequate, the patient should be referred for a direct laryngeal evaluation.

If a diagnosis of a malignancy is suspected, the patient should be admitted for a complete ENT evaluation consisting of direct examination and biopsy. More sophisticated tests such as tomograms, laryngeal contrast studies and a barium swallow all serve to better delineate the lesion and its extension.

Following an accurate visualization of the lesion and any extensions, precise staging is carried out using the American Joint Committee recommendation with the TNM classification.¹ In this classification, T designates tumor extent and is graded 1 through 4. T₁ indicating a small lesion involving one site in a particular region, T₂ involving two sites, T₃ two regions and T₄ extension outside of the larynx. Prognosis, method of therapy and comparative treatment results all are directly related to accurate staging.

PATHOLOGY

The most frequent malignant lesion occurring in the larynx is a squamous cell carcinoma. In the supraglottic region, this is commonly an undifferentiated carcinoma; whereas, those of the glottic and subglottic regions are usually more highly differentiated. It should be recalled that except for the true vocal cord, which is covered by squamous epithelium, the larynx

is lined by columnar epithelium where squamous metaplasia may occur under a variety of circumstances. Adenocarcinoma, lymphosarcomas and other tumors occur rarely in the larynx.

The primary laryngeal lesion infiltrates in all directions and in the supraglottic region may be quite extensive before symptoms bring the patient to a doctor. Ultimately, infiltration extends beyond the larynx to involve cartilage and soft tissues of the neck. Lesions of the epiglottis in particular, extend rapidly into the pre-epiglottic space, a factor of considerable importance in determining treatment. McGavran in his study reported the incidence of lymph node metastasis from the various sites as glottis 0 per cent; subglottis 19 per cent; and supraglottis 33 per cent, which coincides very nicely with the lymphatic drainage from these sites.⁶ Lesions of the supraglottic region frequently metastasize bilaterally.

Blood-borne metastases are unusual, but are seen more frequently these days with better control of the primary disease.

Pre-malignant and in-situ carcinomas of the larynx occur as in the uterine cervix, and require the same care in excluding possible invasion.

TREATMENT POLICY

The formulation of a treatment policy will necessarily be governed by the philosophies and experience of the various members of the cancer team. It must, however, represent a multi-disciplinary effort and be based upon clinical knowledge and current research. Once a policy is established, it should be adhered to and not altered unless good evidence is presented to make a particular treatment plan passe' or another one more promising. Eventually, a significant result may be obtained from a large group of patients treated in a similar manner.

A policy for treatment of the whole spectrum of laryngeal cancer must bear a direct relationship to the staging.

The following suggested treatment outline represents the current policy usually adhered to by the Radiotherapy and Otolaryngologic Departments at the Medical University of South Carolina.

Although radiation therapy and surgery approximate each other in the cure of early laryn-

CANCER OF THE LARYNX

TABLE I
Treatment Policy

I. Supraglottis	
State:	Treatment:
T ₁ A OR T ₁ BNo	Either Definitive Radiotherapy
	or
T ₂ No	Supraglottic Laryngectomy
T ₁	Combined Therapy
T ₂ With Nodes	Prefer 5000 rads
	Pre-operative + Laryngectomy & Neck Dissection
T ₃	Combined Therapy
T ₄	Prefer 5000 rads
	Pre-operative + Laryngectomy & Neck Dissection
II. Glottic (True Vocal Cord Lesion)	
T ₁ A No	
T ₁ B No	Definitive Radiotherapy
T ₂ No	
T ₂ (Fixed) Without Nodes	Partial or Total Laryngectomy
T ₃ With or Without Nodes	Combined Therapy
III. Subglottic Lesions	
	Combined Therapy
	Pre-operative Radiotherapy + Surgery

geal cancer, it is felt that the functional result following radiotherapy is superior to that following surgery. Further, the few cases that may fail with radiation therapy are amenable to salvage by laryngectomy.^{7, 8}

With regard to advanced cancer, the evidence from several centers seems to indicate that the best results are obtained from combined pre-operative irradiation and radical surgery.^{4, 10} Neither the irradiation nor the surgery should be compromised; thus, a relatively high dose, 5,000 rads in five weeks, should be employed followed by total laryngectomy usually with a neck dissection.

With respect to neck dissections, all supraglottic lesions undergoing definitive surgery with or without palpable disease in nodes should have neck dissection in continuity with primary resection. Glottic lesions stage T₃ and T₄ should be managed in the same fashion.

RESULTS OF TREATMENT

Most centers treating substantial numbers of patients with laryngeal cancer report similar

five year survival rates for early supraglottic and glottic lesions regardless of whether definitive radiotherapy or surgery is employed. (Ref. 2 5 7 8)

In the most part, they are in the 85-90 per cent range. Vermund has provided a summary of the results from some twenty investigators and a comparison can be made between radiation and surgery stage for stage.⁹

These results point up the need for conservation in early cases and combined treatment for later cases. Recent reports from Boston, Mt. Sinai Hospital, in New York, and the University of Virginia Hospital reveal a considerable improvement in survival for advanced cancers with the utilization of high dose pre-operative irradiation and surgery.^{3,4,10} The local recurrence rate and the node recurrent rate is markedly reduced and there is an acceptable complication rate, however, more care and attention to sound surgical technique must be practiced when operating upon irradiation tissue.

CANCER OF THE LARYNX

SUMMARY

Cancer of the larynx has an excellent cure rate when discovered in an early stage. Recent advances with combined radiation therapy and radical surgery have remarkably improved the survival percentage even in the advanced

stages. There is now a strong emphasis on a team approach when dealing with this fairly common malignancy and we think the recent improvement in results is indicative of this approach. □

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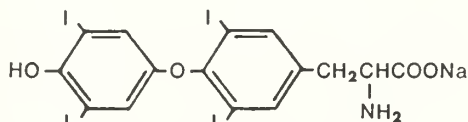
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SYNTHROID (sodium levothyroxine) products serve as specific replacement therapy for reduced or absent thyroid function of any etiology. SYNTHROID **Injection** can be used intravenously whenever a rapid onset of effect is critical, and either intravenously or intramuscularly in hypothyroid patients whenever the oral route is precluded for long periods of time.

Contraindications

There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis. (See WARNINGS)

Warnings

Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions

Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule. With SYNTHROID (sodium levothyroxine) **Tablets**, the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

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Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration

For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0.2 mg) of SYNTHROID (sodium levothyroxine) **Tablets** daily will restore normal thyroid function and only occasionally will patients require larger doses. Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism, special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent onset of hypothyroidism, full replacement dose of 150 mcg (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view of the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patient as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedematous infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 mcg (0.025 mg) per day. Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at three to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration.

Laboratory tests to monitor thyroid replacement therapy are of limited value. Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with the clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occurs and should not be considered evidence of overdosage per se.

In all cases, clinical impression of the well-being of the patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critical importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size, the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROID **Injection** may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsiveness within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred. Like the oral dosage form, SYNTHROID **Injection** produces a predictable increase in the circulating level of hormone with a long half-life. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient is fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

SYNTHROID **Injection** by intravenous or intramuscular routes can be substituted for the oral dosage form when ingestion of SYNTHROID **Tablets** is precluded for long periods of time.

How supplied

SYNTHROID (sodium levothyroxine) **Tablets** are supplied as scored, color-coded compressed tablets in 6 concentrations: 25 mcg (0.025 mg)—orange . . . 50 mcg (0.05 mg)—white . . . 100 mcg (0.1 mg)—yellow . . . 150 mcg (0.15 mg)—violet . . . 200 mcg (0.2 mg)—pink . . . 300 mcg (0.3 mg)—green. Depending on strength, these tablets are available in bottles of 100, 500, 1000 and 5000.

SYNTHROID (sodium levothyroxine) for **Injection** is supplied in 10 ml vials containing 500 mcg of lyophilized active ingredient and 10 mg of Mannitol, U.S.P. A separate 5 ml vial containing Sodium Chloride Injection, U.S.P. is provided as a diluent.

Directions for reconstitution

Reconstitute the lyophilized sodium levothyroxine by aseptically adding 5 ml of the Sodium Chloride Injection, U.S.P. to the vial. Shake vial to insure complete mixing. Use immediately after reconstitution. Discard any unused portion.



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MEDEX South Carolina: A Progress Report

KENNETH J. BUHMEYER, Ph.D.*

ARTHUR C. HUTSON, JR., M.D.**

In 1971 a Medical University Ad Hoc Committee enthusiastically endorsed the concept of developing professional surrogates to improve the quality and quantity of health care delivery in this state. The Department of Family Practice, under the leadership of Hiram B. Curry, M.D., was given the responsibility of implementing this recommendation.

By July 1972, federal funding had been secured from the Bureau of Health Manpower Education for one year to train fifty assistants to primary care physicians.¹ The first class of 19 former military corpsman commenced training in October in the department's MEDEX Physician's Assistant Program.

The MEDEX concept, developed by Richard Smith, M.D., at the University of Washington² emphasizes advanced training of allied health workers within a physician's practice after an initial University program. Medex candidates are selected and matched with practicing physicians who have applied to the program.

The practicing physician acts as a preceptor within the program and orients his Medex to his practice and community. At the end of the one year of intensive training the candidate is certified by the Medical University of South Carolina as an assistant to a primary care physician and is eligible to sit for the National Boards administered by the Board of Medical Examiners. The Medex continues with his preceptor physician as a member of his health team.

In October 1973, 17 candidates were certified by the University and became full fledged

members of their preceptors' practices in South Carolina, Georgia, and Alabama. By June 1974, 68 candidates were in training or certified and working in eight southeastern states under continued federal funding and program sponsorship through the Department of Family Practice and the College of Allied Health Sciences.

In 1973, South Carolina passed legislation governing the physician's assistant under regulations set forth by the State Board of Medical Examiners. Mississippi, Tennessee, and Kentucky are the only southeastern states to date without similar legislation.

The locations of the Medex are varied and reflect the medical care needs of particular communities (Table 1). The majority are working with physicians in rural communities. This may reflect the physician shortage in such locations. Many Medex work in urban areas with various state and federal health care programs. All Medex are directly supervised by their preceptor physician. The majority of Medex are located in the State of South Carolina (Table 2), and it is anticipated that the increase in preceptorship participation by the state's physicians will insure that this continues.

TABLE 1

Distribution of Medex by size of town in which preceptor-physician's practice is located.

Size of Town	Number of Medex
Under 2,500	22
2,500-10,000	27
10,000-99,999	5
Over 100,000	14

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MEDEX SOUTH CAROLINA

TABLE 2

Distribution of Medex by State in which preceptor-physician's practice is located.

State	Number of Medex
Arkansas	1
Alabama	5
Florida	2
Georgia	3
Kentucky	2
Mississippi	3
North Carolina	4
South Carolina	48
TOTAL	68

The sixth MEDEX class commences training on September 30, 1974. The 26 candidates have varied backgrounds in the health professions. The majority are former military corpsmen, as was true for past classes, but more nurses and other allied health professionals have been included in recent classes. The present candidates will study for six rather than three months at the University before beginning a preceptorship in a physician's practice.

A survey of tasks which the Medex performs indicates that he is becoming a viable member of the health care delivery team. The majority

perform in areas of data collection (obtaining histories and performing physical examinations), counseling (management and follow-up of certain chronic problems such as hypertension, diabetes, obesity, substance abuse and pre-natal examinations according to the preceptor's protocols), screening patients to be seen by the physician, management of many minor acute illnesses, and routine procedures for hospitalized patients including the admissions examination, rounds, and preparing discharge summaries.

Many practices have found that the Medex physician assistant can expand and improve health care delivery by giving physicians more time to pursue a particular and complex problem in greater detail or provide new services to their community. New services have included health maintenance programs and expanded interpersonal family counseling. The practice of family medicine has begun to utilize a new health professional who has found a challenge and has made a commitment to primary health care delivery. It is the University's responsibility to evaluate their role and impact on a continuing basis in health care delivery. This is essential if the University is to provide the practicing physician with responsible assistants. □

REFERENCES

1. The primary care physician is one whom the patient generally consults directly, and whose practice is characterized by a broad scope of medical services, including the management of acute problems, chronic illness, preventive and emergency services, and personal and family counseling (AMA's House of Delegates, 1972).
2. Present Address: Department of Community Medicine, University of Hawaii.

A BRIEF HISTORY OF OTOLARYNGOLOGY IN CHARLESTON, SOUTH CAROLINA

R. W. HANCKEL, M.D.*

The Medical College of South Carolina was established by an act of the South Carolina Legislature in 1823 and opened its doors to its first class in November 1824, making it the oldest in the country south of Baltimore and the tenth oldest of the surviving schools.

The faculty was at first entirely a part-time clinical faculty. In fact, it was not until the Administration brought in Frederick Kredel, M.D., as full-time Associate Professor of Surgery in 1937 that we had such a faculty member. In that year also, William Kelley, M.D., became full-time Associate Professor of Medicine and John Boone, M.D., became full-time Instructor in Medicine. All the sub-specialties of surgery and medicine remained under the guidance of clinical chairmen until the 1950's and 60's when they were headed by geographic full-time faculty members. The only exception to this is the Department of Orthopedics whose chairman is a clinical professor.

Otolaryngology remained a division of Surgery until May 1956, when, by action of the Board of Trustees, it was made a separate department along with several other surgical specialties. It remained under a clinical head until 1961 when the present chairman became a member of the full-time faculty, after being in private practice in Charleston for over twenty years.

One of the early practitioners of medicine in Charleston with some interests in otolaryngology was Francis LeJau Parker, M.D. He was born in the old Abbeville district in upper South Carolina in 1836, twelve years after the founding of the Medical College, and died in Charleston at the age of 77, in 1913. He was the major connecting link between the old and the more modern faculty. He graduated from The

Citadel in 1855 and from The Medical College of The State of South Carolina in 1858, having also studied medicine during these years in the office of his uncle, Professor Henry R. Frost.

Dr. Parker was appointed a house officer at Roper Hospital after his graduation and served during the yellow fever epidemic of that year. He contracted this dread disease himself while at Roper. After finishing his internship, he began the practice of medicine in Charleston and was appointed Demonstrator of Anatomy under those distinguished instructors, Professors Holbrook and Miles.

The War Between the States interrupted his practice of medicine. He saw action in this war when it began with the firing of the first shot at Fort Sumter in April 1861. At that time



F. L. Parker, M.D.

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he was Assistant Surgeon of the South Carolina Volunteers stationed at Morris Island. He afterward served with distinction first as Assistant Surgeon under Commodore Page, Confederate States Navy, at Chapin's Bluff, James River, below Richmond. Desiring more active service, he obtained a transfer as surgeon of the Hampton Legion Infantry, Army of Northern Virginia. He later was appointed chief surgeon of this division, and served until the retreat to Appomattox.

After the war he returned to Charleston and resumed the practice of medicine. He renewed his contact with his alma mater during this critical post-war period. In 1866 he was appointed Demonstrator of Anatomy and four years later succeeded to the full professorship. He devoted special attention to diseases of the eye and ear, and in 1882 became Clinical Lecturer on these subjects.

In 1891 he was elected Dean of The College and remained in this position until he retired in 1906.

Dr. Parker was the author of numerous articles on general surgery and also on diseases of otolaryngology in which he was particularly interested. He operated under chloroform anesthesia on a patient having a Bezold's abscess in December 1875, using a post-auricular incision and an incision along the anterior border of the sterno-cleido-mastoid muscle to drain the abscess. One of his most important contributions was on the suturing of divided nerves, in which field he was a pioneer.

He was past president of the Medical Society of South Carolina, the first society of organized medicine in South Carolina, founded in 1789, and of the South Carolina Medical Association. The degree of LL.D. was conferred upon him by the University of South Carolina at its centennial celebration in 1905.

During his deanship the sessions were lengthened from two to three years and then to four, laboratory facilities were expanded, the College of Pharmacy was established, and women were admitted to the practice of medicine.

Another early practitioner of otolaryngology in Charleston was Charles Wilson Kollock, M.D. He was born in Cheraw, South Carolina, April 29, 1857, the son of one of the South's distinguished surgeons. He entered Virginia Military Institute and was graduated in the



Charles Wilson Kollock, M.D.

class of 1877. He read medicine in the office of his father for a year and then entered the Medical College at the University of Pennsylvania, graduating in 1881. He did post-graduate training at the Philadelphia Hospital for one year and at Children's Hospital for six months. Following this, he was a resident at Wills Eye Hospital for a year. He then pursued further training for a year and a half in the field of otolaryngology at the clinics in London and Paris.

He opened his office in Charleston in June 1885 and practiced his specialty there until a long terminal illness forced his retirement. He died in 1931.

Among the honors which came his way was the Presidency of the South Carolina Medical Association in 1898. After this he was elected a delegate to the American Medical Association and, as such, was appointed member of a committee to raise funds for a monument to Benjamin Rush. He later participated in the unveiling of this monument in Washington during the presidency of Theodore Roosevelt.

He was a clinical appointee in rhinology and laryngology on the Medical College faculty.

Another of the early specialists in otorhinolaryngology in Charleston was Walter Peyre Porcher. He was born in Charleston, February

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25, 1858, the son and grandson of physicians. He was a graduate of Union College and in 1881 he graduated from The Medical College of South Carolina with high honors. He went immediately into the private practice of general medicine in Charleston, and then in 1887 he traveled to Vienna where he did post-graduate study in diseases of the Eye, Ear, Nose, and Throat. He then returned to Charleston and practiced his specialty until the time of his death in 1919.

He was a president of the Medical Society of South Carolina and the South Carolina Medical Association. He was a member of The American Laryngological Association, and the American Laryngological, Rhinological and Otolological Society (Triological Society).

When Dr. Porcher was president of the South Carolina Medical Association in 1900, he recommended in his presidential address the establishment of a state medical journal. There had been no medical journal published in South Carolina since 1877 because of the slow post-war recovery. This suggestion was implemented under the presidency of Dr. Robert Wilson in 1905 and The Journal began its career in June, 1905 with Dr. Wilson himself as editor-in-chief.

He was the author of thirty scientific publications, most of them published in the Journal

of the South Carolina Medical Association. Several of them deserve special mention.

In his article on "Syphilis of the Ear," Dr. Porcher, who was quite a wit, mentioned that mercury powder used in the treatment of gummas of the auricle, may be said to be converted into silver, and at the same time transferred from the patient's pocket into that of the physician.

In this same article, he advised a patient to put nothing smaller than his elbow in his ear, an expression that the author had heard many times in private practice, but had never seen before in print.

"True Catarrh — Its Proper Etiology and Treatment," deals only with "catarrh" of the nose and nasopharynx and not of the middle ear. "Catarrh" of the middle ear was a misnomer originally applied to all types of chronic deafness including otosclerosis. In this article the catarrh was thought to be the precursor of atrophic rhinitis and ozena, a condition more prevalent in those days.

"Subcutaneous Plastic Surgery of the Nose," published in 1910, deals with the beginnings of rhinoplasty as it is practiced today. The method was popularized in this country by Dr. John O. Roe of Rochester, New York, whom Dr. Porcher quotes extensively. Dr. Jacques Joseph of Berlin, one of the early pioneers on this subject, published his textbook on Rhinoplasty in 1928 in Leipsig. It is of interest that Dr. Roe is lost in limbo, whereas Dr. Joseph's fundamental principles are the basis from which modern rhinoplastic surgery has developed.

"The Prevention of Colds and Their Sequelae by Surgical Methods" advocates the removal of nasal obstructions and the restoration of the lumen of each nostril "and removing centres of reflex irritation" by septoplasty and other surgical procedures. In this paper the author mentions Dr. Daly of Pittsburgh as being one of those who believes that hypertrophy of the anterior tips of the turbinates is a cause of hay fever.

"Should the Tonsils Be Removed?" deals with this question when the pendulum was at the top of its swing in the craze for performing the operation of adeno-tonsillectomy. Some quotations were "it is easier to enucleate than to investigate," and "the man who tonsillectomizes a dozen or fifteen patients in a



Walter Peyre Porcher, M.D.



John L. Dawson, M.D.

single afternoon, had better spend his afternoons in the abattoir." Porcher advocated the use of the Sluder tonsillotome and the removal of tonsils that were enlarged enough to project beyond the pillars of the fauces.

John Lawrence Dawson, M.D., embraced two specialties, Ob-Gyn, and EENT. He was born in Charleston September 29, 1856, the son of a well-known physician.

He graduated from the College of Charleston in 1878 with the degree of Bachelor of Arts and from The Medical College of The State of South Carolina in 1881. The College of Charleston conferred the degree of Master of Arts on him at that time.

In 1887 he was elected Demonstrator of Anatomy at the Medical College. In 1883-84 he was Clinical Assistant in Eye and Ear and in 1888-90 Clinical Lecturer of Diseases of the Eye and Ear. He was Assistant Professor of Gynecology and Obstetrics from 1887-1888. He became Professor of the Practice of Medicine from 1890-1904, and again from 1913-1915. He was Emeritus Professor from 1915 to his death in 1917.

He contributed some ten papers to the medical literature, among them being a particularly profound address on "The Need of Better Education in The Preparation for The Study of Medicine."

Dr. Dawson was well-known as a practitioner and diagnostician, in which latter role he excelled. He was particularly interested in tuberculosis, being President of the National Association for the Study of Prevention of Tuberculosis. He was also secretary of the South Carolina Medical Association for ten years and its president in 1909. He was also President of the Medical Society of South Carolina, 1908-10.

Edward Frost Parker, M.D., was the first professor of ophthalmology and otology at the Medical College of The State of South Carolina. He was born in Charleston, December 16, 1867, a son of Francis LeJau Parker, M.D.

He received his pre-medical education at The Citadel and the University of Virginia. He was the first honor graduate in medicine at the Medical College of The State of South Carolina in 1889. After graduation he practiced medicine in Charleston for six years.

In 1895 he went to London where he studied diseases of the eye, ear, nose, and throat at the Royal London Ophthalmic Hospital and the Golden Square Nose and Throat Hospital. On his return to Charleston he confined his practice to his specialty. He was elected Professor of Diseases of the Eye and Ear in 1911 and became Professor of Ophthalmology and



Edward F. Parker, M.D.

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Otology in 1913 when the College became a State institution.

He was elected dean of the Medical College in 1906, succeeding his father. He served in this capacity for three years, resigning because of the press of other duties.

He was president of the South Carolina Medical Association and the Medical Society of South Carolina, both in the same year, 1914.

In 1935 he invited the American L.R. and O. Society (The Triological Society) to meet in Charleston and they accepted, naming Dr. Parker an Honorary Fellow on June 2, 1935. This was the only time the National Society ever met in Charleston, although the Southern Section met here in 1965 on the author's invitation.

He was the author of about thirty scientific publications, most of them relating to luetic and other infections of the eye, ear, nose, and throat.

He retired as Professor, Ophthalmology and Otology in 1935 and became Professor Emeritus. He died in Charleston in 1938.

John Ferrars Townsend, M.D., succeeded E. F. Parker, M.D., as Chairman of the Division of Ophthalmology and Otolaryngology in 1935 and served in that capacity until he retired in 1950.

He was born on Edisto Island, April 22, 1880.



John F. Townsend, M.D.



Pierre G. Jenkins, M.D.

He attended Presbyterian College and was graduated from The Citadel in 1899. He received his M.D. degree from The Medical College of the State of South Carolina in 1903.

He was president (1943) of the Medical Society of South Carolina. He was a member of The South Carolina Medical Association, The American Medical Association, and a Fellow of the American Academy of Ophthalmology and Otolaryngology. He was also a Fellow of the American College of Surgeons.

He was the author of fourteen papers published in the medical literature, relating to diseases of the eye, infections of the ear, and medical history.

He died in Charleston January 31, 1962.

After Dr. Townsend's retirement in 1950 the departments of ophthalmology and otolaryngology were separated, Pierre G. Jenkins, M.D., becoming Chairman of the Department of Ophthalmology and Robert M. Hope, M.D., Chairman of Otolaryngology.

Robert M. Hope, M.D., was born March 5, 1903, at Lockhart, South Carolina, the son of a physician. He graduated from the University of South Carolina in 1923. Following graduation he worked for the University Alumni Association for two years before entering the Medical College of The State of South Carolina. He graduated in 1928. He interned at Roper Hospital for a year and entered a pre-



Robert M. Hope, M.D.

ceptorship under Josiah E. Smith, M.D., in eye, ear, nose, and throat. Later, he entered private practice in his specialty in Charleston.

Dr. Hope served as Chairman of the Department of Otolaryngology from 1950 until his retirement in 1961. During his chairmanship, the Division of Otolaryngology became the Department of Otolaryngology operating on equal basis with the other departments, the chief administrative officer being known as the Chairman.

Upon retirement in 1961 he became Emeritus Professor of Otolaryngology and remained in this position until his death June 27, 1964.

Before considering the more recent history of otorhinolaryngology in Charleston, the author would like to mention some of the clinical members of the staff of otorhinolaryngology who were in practice when he had returned to Charleston in October 1940.

Josiah Edward Smith, M.D., mentioned above, was born in Charleston, South Carolina, November 2, 1889, a son of John North Smith and Margaret Ballantyne Sinkler Smith.

He attended the College of Charleston and received the degree of bachelor in pharmacy from the Medical College of the State of South Carolina. In 1916 he received the degree of doctor of medicine from Jefferson Medical College in Philadelphia, Pennsylvania.



Josiah E. Smith, M.D.

After graduation at Jefferson he served an internship at Jefferson Medical College Hospital and then did post-graduate studies in ophthalmology and otorhinolaryngology at the same hospital.

He began the combined practice of ophthalmology and otorhinolaryngology in Charleston in 1920, and became a member of the clinical staff at the Medical College of the State of South Carolina at a time when there was no full-time faculty in these specialties there. He gave generously of his time and efforts and served as clinical professor of ophthalmology and otorhinolaryngology from 1937 to 1940. He resigned as professor of otorhinolaryngology in 1940 but continued on as professor of ophthalmology until 1944. He confined his practice to ophthalmology alone from 1940 until his death in 1961.

Two physicians served their preceptorships under him. One was Dr. Hope, as noted above. He was with Dr. Smith from 1929 to 1936. The other was Clay W. Evatt, M.D., who was associated with him from 1936 to 1940.

Dr. Smith was a member of Kappa Alpha and the medical fraternities Phi Alpha Sigma and Alpha Omega Alpha.

He died September 14, 1961, at his residence, 78 East Bay Street in Charleston, and was buried in Magnolia Cemetery.

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Clay Welborn Evatt, M.D., was engaged in the private practice of ophthalmology and otorhinolaryngology when the author returned to Charleston in 1940. He also served ably in the clinics of Roper Hospital and as lecturer on subjects relating to his specialty while in practice in Charleston.

Dr. Evatt was born in Anderson County in South Carolina, September 16, 1898. He was educated in Anderson County Schools, and the Epworth Orphanage High School. He received his B.A. degree from the University of South Carolina and his M.D. degree from the Medical College of Virginia in Richmond in 1924. He interned at St. Luke's Hospital and McGuire Clinic in Richmond. He started the general practice of medicine in Greenville, South Carolina, in 1925 and remained there ten years. He was particularly interested in problems relating to tuberculosis at that time, having graduated from the Trudeau School of Tuberculosis in 1926. He started, with Miss Mamie Oetsel, the first tuberculosis clinic for blacks in South Carolina.

He moved to Charleston in 1935 and became associated with Dr. J. E. Smith in the practice of ophthalmology and otolaryngology. He remained with him several years before opening an office of his own for the private practice of ophthalmology. He was subsequently joined by his son, Clay Evatt, Jr., in the practice of ophthalmology. The son is still in practice in Charleston.

Dr. Evatt became Clinical Professor Emeritus of Ophthalmology at the Medical College of South Carolina in 1967. He died in Charleston, January 31, 1969.

Still another clinician who worked diligently in the clinics and classrooms for thirty years, from 1937 to 1967, was F. Raymond Price, M.D.

Dr. Price was born in Charleston, South Carolina in 1896. He was graduated from the Medical College of the State of South Carolina in 1922 and, interestingly enough, did not receive his B.S. degree from the College of Charleston until ten years later in 1932.

From 1924 until 1931 he was appointed Assistant in Medicine at the Medical College. He transferred his interests to surgery and became Assistant in Surgery from 1931 until 1934. He then spent two years in post-graduate training at the Massachusetts Eye and Ear Infirmary, 1934-1936.

He returned to Charleston and entered the combined practice of ophthalmology and otolaryngology from 1936 until 1955. After this, he restricted his practice to ophthalmology.

Dr. Price rose from a Lecturer in Eye and Otorhinolaryngology in 1937-38 to Professor Emeritus of Ophthalmology, 1967-1974. He died December 10, 1974.

A very colorful practitioner of otolaryngology who is pleasantly recalled by the author is R. Barnwell Rhett, M.D.

Dr. Rhett was born in Charleston, South Carolina, August 6, 1890, the son of Robert Barnwell Rhett, M.D., of Charleston, and Margaret Butler Cornell Rhett, a native of New Jersey.

He graduated from Virginia Military Institute in 1910 and from the Medical College of the State of South Carolina in 1914. He interned at Methodist Hospital in Brooklyn, New York, and had a post-graduate session at Harvard Medical School.

He entered the armed forces as a volunteer in the British Army at the grade of a First Lieutenant. In March of 1917 he was captured and made a prisoner of war by the Germans. He spent the remainder of his service in concentration camps mostly in Belgium caring for English soldiers.

After the Armistice he returned to Charleston and entered the practice of general medicine for a year with Dr. Joseph Maybank. He then practiced general medicine until 1928 when he took post-graduate studies in eye, and ear, nose, and throat at Bellevue and New York Eye and Ear Hospital in New York City.

Dr. Rhett returned to Charleston and practiced his specialty, until the time of his death. He died suddenly at his mountain home near Flat Rock, North Carolina, on March 23, 1943.

At the time of his death at the age of 52, he was a Clinical Associate in Ophthalmology at the Medical College of the State of South Carolina.

The author succeeded Dr. Hope as Professor and Chairman of the Department of Otolaryngology on July 1, 1961. On that date he moved his office within the geographic confines of the Medical University Hospital, thus becoming the first geographic full-time occupant of that Chair.

At the present time the Department consists of two members of the geographic full-time

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staff other than the author. They are F. Johnson Putney, M.D., Professor of Otolaryngology, and Warren Y. Adkins, M.D., Assistant Professor of Otolaryngology. Dr. Putney has a national and international reputation in his chosen field which is primarily cancer surgery of the head and neck. Dr. Adkins who joined our staff on July 1, 1972, has participated vigorously in departmental activities and, as a result of his efforts, we have established a temporal bone laboratory and an electronystagmographic laboratory for evaluating the dizzy patient. We also have a Division of Audiology and Speech Pathology under the able direction of Dr. Daryle Waldron. Dr. Clark Donley is a member of our research staff and is presently engaged in basic research on taste and smell.

An active member of the clinical part-time staff is A. Lawrence Lemel, M.D. He and those in his group are doing yeoman service in the clinics and in the dissecting laboratory, helping with the instruction of our resident staff.

In the consortium group we have Frank Wier, M.D., L. R. Hurst, A.B., M.D. and D. G. Stowe, A.B., M.D., of Spartanburg. Other members of the consortium group are from Greenville, Anderson, and Columbia. They are: W. Steve Lang, M.D., Greenville; Juan A. Brown, M.D., Anderson; James M. Timmons, M.D., Columbia; James F. White, M.D., Columbia.

In the immediate future, we hope to acquire the services of a director of research and resident education at the Ph.D. level. We also plan to increase our geographic full-time medical faculty by one to a total of four and our resident staff from eight to twelve.

In the more distant future, we will move our physical plant from our present cramped quarters on the second floor of the Medical University Hospital to more adequate space in the Clinical Science Building whose framework is now making its appearance in our medical complex. □

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President's Pages



November 7, 1975

Dear Fellow Physicians:

Recently, Dr. Stanley E. Gitlow of New York talked to the Scientific meeting of the Columbia Medical Society about the problem of the sick physician. Dr. Gitlow has a long background of experience in handling the problems of the physician who has been impaired by disorders, including alcoholism and drug dependence. His was a most informative and startling revelation of the magnitude of the problem among the physician population. He stated that, at some time or other in their life, 10% of all physicians have some degree of this problem. He also stated that this was a nationwide statistic, not true just for the state of New York.

The timeliness of this discussion was emphasized to the members of the Columbia Medical Society by the fact that one of our younger physicians had died most recently under distressing circumstances. The tragedy of this struck home to all of us in this area and, in looking back, many other names could be added to this list as having had some problem resulting in death or suicide, or lack of ability to practice medicine.

When one of us, as a practicing physician, gets a phone call from a tearful distraught patient asking what can she do because her doctor is gone, stating that she can not believe the rumors and "knows that this just couldn't have happened that way," she has lost her trusted medical advisor and does not know to whom to turn, the seriousness of the problem strikes home.

It is the duty of organized medicine and of each physician to realize that it is a physician's ethical responsibility to take cognizance of a colleague's inability to practice medicine adequately, by reason of physical or mental illness, including alcoholism or drug dependence. Therefore, the Council of the South Carolina Medical Association was requested to establish an ad hoc committee to be composed of interested and dedicated physicians who might study this problem as it relates to us in South Carolina. This Committee will be appointed soon.

Dr. Gitlow brought out in his discussion the methods used in New York State, and also gave us a copy of the New York State law setting up a legal commission to handle the problem. The emphasis on their approach was the privacy and anonymity of the approach to the involved physician. The Chairman of the Committee would receive the complaint about the individual physician. He would appoint two or three physicians who would not be involved in everyday contact with the individual physician. This Committee would not be known to anyone else, and would privately call the physician involved for an appointment and meet with him, in private. All of their discussion would be private, with no written record kept. The thrust of this interview would be to help the physician in need of help and not to attempt, in any way, to punish or coerce him into a course of action.

Dr. Gitlow referred to the JAMA of February 5, 1973, Volume 223, Number 6, page 684, an article entitled "The Sick Physician - Impairment by Psychiatric Disorders, Including Alcoholism and Drug Dependence" from the Council on Mental Health of the American Medical Association. At the end of this article are various references, nine in number, which are available for further perusal.

In these days of physician liability problems, the public and the legislators are looking to the medical profession to clean house and eliminate the problem doctor who is not practicing competent medicine. In the South Carolina Medical Liability Study Committee, Don Kilgore and I are being asked to come up with recommendations to this Committee for disciplinary measures to be used within our profession.

As you know, at the May Convention we passed, after great discussion, a model disciplinary Act to be presented to the Legislature. This original draft has been tabled by the Medical Affairs Committee of the S. C. House of Representatives because the Attorney General declared it unconstitutional. A second draft was then prepared which, again, was declared by the office of the Attorney General as not meeting constitutional requirements. Two members of the Staff of the Attorney General met with Council and have since been working with the legal representative of our Association in preparing a further draft of this legislation. Your President and your Secretary, Strother Pope, with Charlie Johnson and the legal representative, met with the Attorney General and his Staff on November 4, 1975, to work out the discrepancies in the present Bill. This proposed legislation will be discussed with the State Board of Medical Examiners on November 9, 1975, and will be presented to the House of Delegates at the meeting of November 15 and 16, 1975.

It is my opinion that this particular Disciplinary Act will not focus thoroughly enough on the problem of the sick physician. Therefore, an ad hoc committee is being appointed to study this problem in depth and will be furnished all the necessary background material that has been done by the AMA and various other State Associations to help it in its work.

Again, may I ask each of you to refer to the February 5, 1973, issue of the JAMA, Volume 223, Number 6, to the article on "The Sick Physician."

If any of the members of the Association have any interest or desire to serve with this Committee, please let me know.

The sick physician is a vital area of concern to each and every medical doctor practicing in our state. Physicians strongly resist recognition of the fact that any of their number can become ill. Their referral for help should not reveal an entrenched conspiracy of silence, but colleagues of the ill practitioner should be willing to speak out, substituting perhaps a conspiracy of constructive compassion.

Experience in such situations is often disappointing as a physician patient denies he is ill, lacks insight to his problem, avoids medical assistance, and minimizes his problem outright.

Therefore, as President of the South Carolina Medical Association, I call upon each of you to recognize our primary responsibility for insuring safe competent care to the patient population. Your concern and help are urgently needed to let each and every one of us develop some insight and help to provide an adequate structure within the framework of the South Carolina Medical Association to effectively cope with this problem.

Sincerely yours,
C. Tucker Weston, M.D.
President



Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

and useful in the management of vertigo* associated with
affecting the vestibular system.
relieve nausea and vomiting often associated with vertigo.*
adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.
available as Antivert (meclizine HCl) 12.5 mg. scored
for dosage convenience and flexibility.
Antivert/25 (meclizine HCl) 25 mg. *Chewable Tablets* for
nausea and vomiting and dizziness associated with motion sickness.

SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS. Based on a review of this drug by the National Academy of
Medicine—National Research Council and/or other information, FDA has classified
indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with
motion sickness.

Probably Effective: Management of vertigo associated with diseases affecting the
vestibular system.

Ineffective: Management of the less than effective indications requires further
evaluation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during preg-
nancy or to women who may become pregnant is contraindicated in view of the
teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation
has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./
kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate.
Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hyper-
sensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients
should be warned of this possibility and cautioned against driving a car or operating
dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children
have not been done; therefore, usage is not recommended in the pediatric age group.

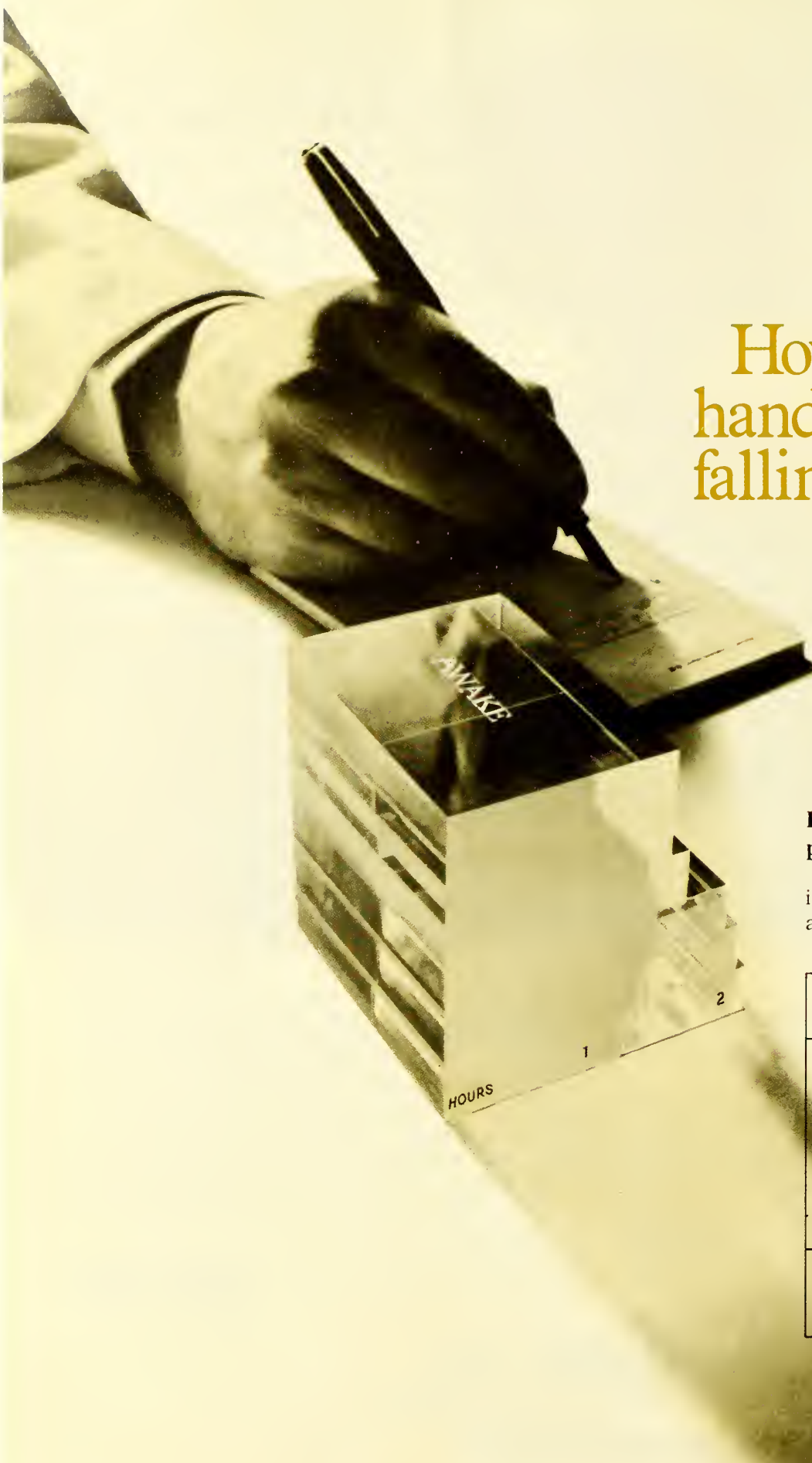
Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred
vision have been reported.

More detailed professional information available on
request.

ROERIG **Pfizer**
A division of Pfizer Pharmaceuticals
New York, New York 10017

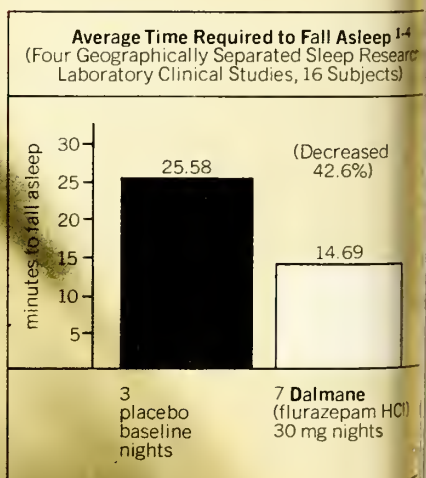
Antivert[®]/25
(meclizine HCl) 25 mg. Tablets
for vertigo*



How do you handle trouble falling asleep?

With Dalmane® (flurazepam HCl), results are highly predictable.

As demonstrated below, Dalmane induces sleep within 17 minutes, on average:¹⁻⁴



And for those with trouble
going asleep or sleeping
enough...

Sleep research laboratory
studies prove: Dalmane
reduces number of nighttime
awakenings and increases total
sleep time.⁵

Dalmane (flurazepam HCl)
is relatively safe, seldom
causes morning "hang-over"

Dalmane is generally well
tolerated. The usual adult dose of
Dalmane should initially be lowered to
15 mg for the elderly and
debilitated, to help preclude
sedation, dizziness or ataxia.
Assessment of possible risks is
suggested before prescribing.

REFERENCES:

1. Macan I, Williams RL, Smith JR:
Sleep laboratory in the investigation
of sleep and sleep disturbances. Scientific
exhibit at the 124th annual meeting of the
American Psychiatric Association,
Washington DC, May 3-7, 1971

2. Roth JD Jr: A system for automati-
cally analyzing sleep. Scientific exhibit at
the 24th annual Clinical Convention of the
American Medical Association, Boston,
Mass., Dec 2, 1970; and at the 42nd
annual scientific meeting of the Aerospace
Medical Association, Houston, Apr 26-29,

1971. GW: Data on file, Medical Depart-
ment, Hoffmann-La Roche Inc., Nutley NJ

3. Bennett WC: Data on file, Medical
Department, Hoffmann-La Roche Inc.,
Nutley NJ

4. Data on file, Medical Department,
Hoffmann-La Roche Inc., Nutley NJ

5. When prescribing Dalmane (flurazepam
HCl), please consult complete product
literature, a summary of which follows:

Indications: Effective in all types of insomnia
characterized by difficulty in falling asleep,
frequent nocturnal awakenings and/or early
morning awakening; in patients with recurring
insomnia or poor sleeping habits; and in
patients with chronic medical situations requiring
sleep. Since insomnia is often transient
and intermittent, prolonged administration is
usually not necessary or recommended.

Contraindications: Known hypersensitivity
to flurazepam HCl.

Warnings: Caution patients about possible
combined effects with alcohol and other
CNS depressants. Caution against hazardous
occupations requiring complete mental alert-
ness (e.g., operating machinery, driving).
Use in women who are or may become preg-
nant only when potential benefits have been
weighed against possible hazards. Not
recommended for use in persons under 15
years of age. Though physical and psycho-
logical dependence have not been reported
on recommended doses, use caution in
administering to addiction-prone individuals
or those who might increase dosage.

Precautions: In elderly and debilitated, initial
dosage should be limited to 15 mg to preclude
oversedation, dizziness and/or ataxia. If
combined with other drugs having hypnotic
or CNS-depressant effects, consider potential
additive effects. Employ usual precautions
in patients who are severely depressed, or
with latent depression or suicidal tendencies.
Periodic blood counts and liver and kidney
function tests are advised during repeated
therapy. Observe usual precautions in
presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness,
lightheadedness, staggering, ataxia and
falling have occurred, particularly in elderly

or debilitated patients. Severe sedation,
lethargy, disorientation and coma, probably
indicative of drug intolerance or overdosage,
have been reported. Also reported were
headache, heartburn, upset stomach, nausea,
vomiting, diarrhea, constipation, GI pain,
nervousness, talkativeness, apprehension,
irritability, weakness, palpitations, chest
pains, body and joint pains and GU
complaints. There have also been rare
occurrences of leukopenia, granulocyto-
penia, sweating, flushes, difficulty in
focusing, blurred vision, burning eyes,
faintness, hypotension, shortness of breath,
pruritus, skin rash, dry mouth, bitter taste,
excessive salivation, anorexia, euphoria,
depression, slurred speech, confusion,
restlessness, hallucinations, and elevated
SGOT, SGPT, total and direct bilirubins
and alkaline phosphatase. Paradoxical
reactions, e.g., excitement, stimulation and
hyperactivity, have also been reported in
rare instances.

Dosage: Individualize for maximum beneficial
effect. *Adults:* 30 mg usual dosage; 15 mg
may suffice in some patients. *Elderly or
debilitated patients:* 15 mg initially until
response is determined.

Supplied: Capsules containing 15 mg or
30 mg flurazepam HCl.

You can
depend on the
efficacy of

Dalmane®
(flurazepam HCl)

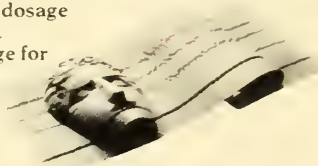
One 30-mg capsule *h.s.*— usual adult dosage
(15 mg may suffice in some patients).

One 15-mg capsule *h.s.*— initial dosage for
elderly or debilitated patients.

for insomnia

Objectively proved in the sleep research laboratory:

- sleep within 17 minutes, on average
- sleep with fewer nighttime awakenings
- sleep for 7 to 8 hours, on average,
with a single *h.s.* dose



ROCHE

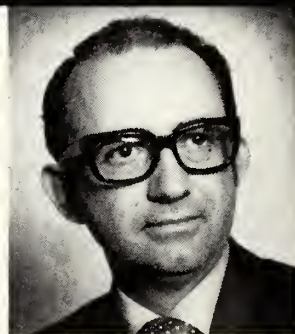
ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

the purpose of drug information to the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with the agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progestone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a longer one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and be removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Or the doctor can remove that fear by 10 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him about a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005



CHILD MENTAL HEALTH UNIT OPENS IN ATLANTA

The first private, comprehensive in-patient psychiatric service for children in Georgia has opened at Peachtree and Parkwood Mental Health Center and Hospitals in Atlanta, Georgia. Out-patient services and a day-care program are an integral part of this new service for children under 13 years of age.



TREATMENT PLAN

A multi-modality approach to psychiatric treatment is used and a comprehensive treatment plan is developed for each child. Psychiatric history, physical and neurological examinations, social history, educational evaluation and psychological testing determine the basic data upon which a treatment plan is devised.

The following types of treatment are used: individual psychotherapy (play therapy); group activities and group therapy; chemotherapy; parents and family therapy, and occupational, recreational, and music therapies. Special emphasis is placed on the family therapy process and treatment involves the family at every step.

MEDICAL SERVICES

Each child admitted receives a complete physical and neurological examination performed by the Center's pedia-

trician. This includes a medical history and necessary laboratory procedures, such as EEG, EKG, and fluoroscopic X-ray studies.

STAFF

The new Child Service is directed by a fully-trained child psychiatrist who has had previous experience with the direction of a child unit. Ten child psychiatrists and several child psychologists are involved in the program, and the staff works as a team in diagnosis, treatment and rehabilitation under the direction of a child psychiatrist.

NEEDED SCHOOLING AVAILABLE

An educational evaluation determines the prescriptive teaching each child requires in the special educational program which is provided.

Peachtree and Parkwood is a comprehensive mental health center which includes alcohol rehabilitation and drug treatment as well as psychiatric treatment for adults, adolescents and children. Complete information on services and facilities may be obtained by writing or calling the Admissions Director:



PEACHTREE and PARKWOOD MENTAL HEALTH CENTER and HOSPITALS

1999 Cliff Valley Way, N.E. Atlanta, Georgia 30329 404/633-8431

Accredited by the Joint Commission on Accreditation of Hospitals

Editorials

Potpourri

This title word comes from the French which originally meant pot of putrescence, which came to be applied to a jar of flower petals and spices, and, from this, a general mixture of disparate material. I intend the third meaning. Perhaps you will think the original meaning is more appropriate. At any rate, this editorial will be a random mixture of ideas of others and of mine; not very thoroughly thought out or espoused here.

1) Have you ever been at Death Valley, or Williams-Brice Stadium, or Carolina Coliseum and heard "Dr. Number So-and-So call answering service" and searched your memory for your number and wondered if you were missing an important call? Most of us have some trouble remembering our numbers, especially during a thrilling play. Ed Bradley has made what seems like a sensible suggestion. Instead of having a special list of numbers, which often change and which often are not available, Bradley thinks it would facilitate emergency calls to standardize numbers all over the state and use the physician's state registration number at all times. We all have a four-digit registration number and probably could learn this in a few years and then not need any other. I think this is a good idea. Maybe somebody would like to push it.

2) Published elsewhere in this issue are excerpts from a meeting of the minds between Executive Committee of SCMA and representatives of S.C. Pharmaceutical Association. The Pharmaceutical Association made some observations which were generally endorsed, at least for consideration, by our leaders. Briefly, these suggestions are:

Physicians refer to Medicaid drug formulary when writing prescriptions for Medicaid patients to insure that their patients get the medicine needed.

Medicaid patients be required to pay fifty cents for each prescription and per-

haps for physicians' fees. This would help defray costs and might discourage over utilization.

Physicians not write more than one drug on the same prescription blank.

Drug names be put on all prescription blanks.

A regulation which would require that prescriptions be telephoned to the pharmacist by physicians only.

We suggest you refer to the excerpts of the minutes and give this your consideration. It is a good feeling to know that our leaders are talking openly and constructively with leaders of other professions. This is how it should be.

3) It is good to hear from Tom Parker again, with his report from the 1975 annual meeting of the American Association of Physicians and Surgeons. He very ably represents one perspective on medical affairs and this is a very viable and respectable perspective, supported by many doctors.

4) Pharmaceutical manufacturers have been under heavy fire these days from federal agencies and consumer advocates for excessive promotion, over pricing, unsubstantiated claims, and other real or imagined transgressions. In this cacophony, a good deed is noteworthy. The makers of an ampicillin, trade-named Larocin, made a very expensive change in the name to Larotid. This required expensive advertising, written notice to all physicians, and the discarding of a tradename with an established identity which had appeared on more than a million prescriptions. This rather magnanimous decision was made because a few pharmacists were known to have misread Larocin prescriptions and dispensed Lanoxin instead.

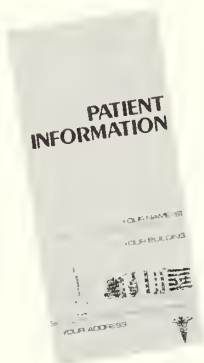
Actions like this and some others mentioned in this issue make you realize the world isn't all bad after all.

EEK

ARE YOUR PATIENTS IN THE DARK?

Do your patients know all they should know about your practice and how it can help meet their needs?

If not you should consider our **PATIENT INFORMATION** brochure created by The R. L. Bryan Company and especially designed to let your patients know exactly what your practice does and does not offer.



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IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdose or individual hypersensitivity, reactions similar to those after meperidine or morphine overdose may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdose; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdose: Keep the medication out of the reach of children since accidental overdose may cause severe, even fatal, respiratory depression. Signs of overdose include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

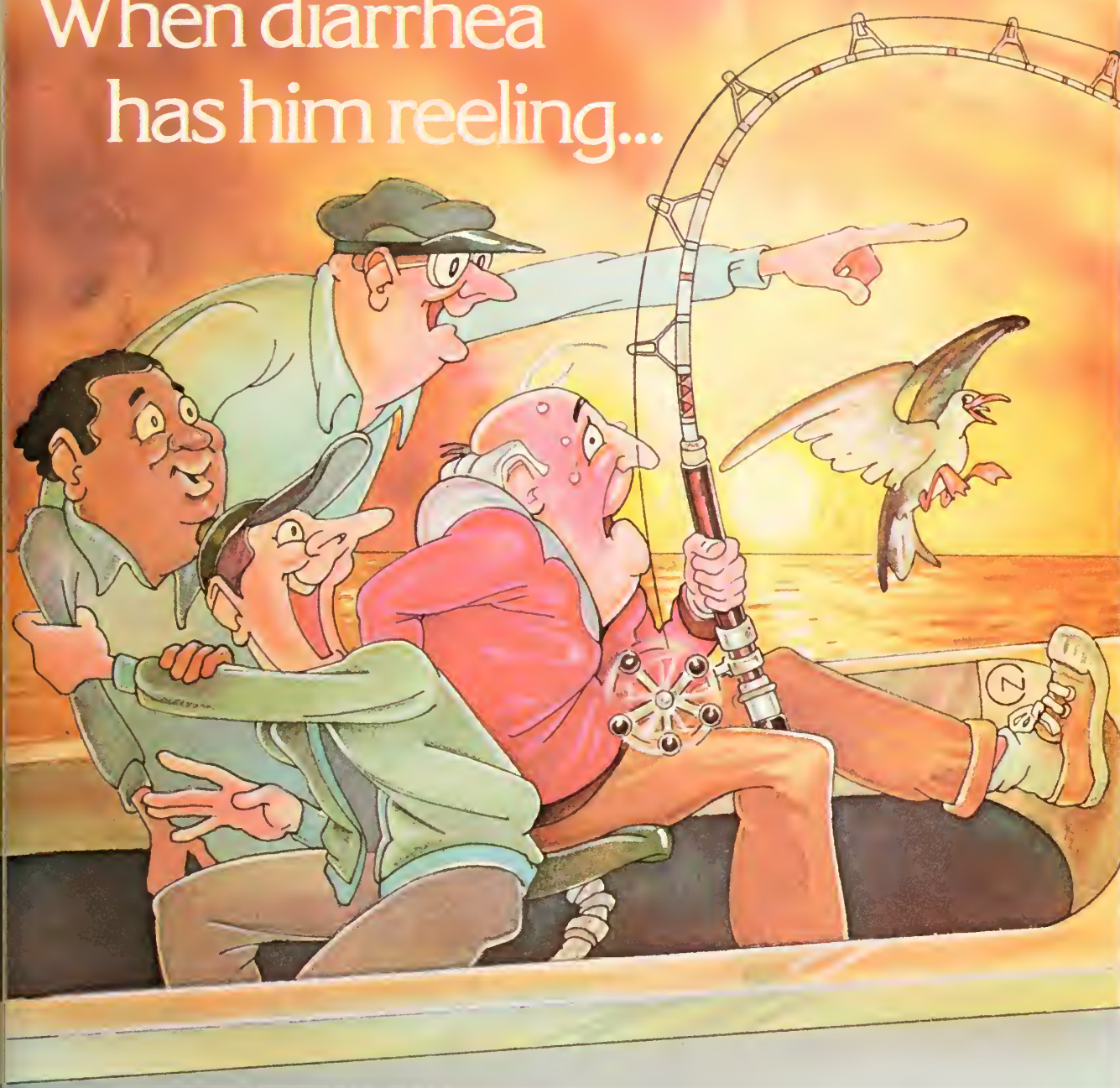
SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

455

When diarrhea has him reeling...



Diarrhea can hook anyone. When it does, physicians and patients both want prompt control of diarrheal symptoms. Lomotil will usually control diarrhea promptly.

This rapid action can halt the emergency aspect of diarrhea and is comforting and reassuring to the patient. Electrolyte and

fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate specific therapy should be given along with Lomotil.

Lomotil is contraindicated in children less than 2 years old.

Lomotil[®]

TABLETS LIQUID

holds the line.

Each tablet and each 5 ml of liquid contain diphenoxylate hydrochloride 2.5 mg (Warning: May be habit forming), atropine sulfate 0.025 mg

In hypertension,

ALDOMET[®] (METHYLDOPA|MSD)

usually offers more
than effective lowering
of blood pressure...



**With ALDOMET
(Methyldopa, MSD),
existing renal function
is usually unchanged**

ALDOMET has no direct effect on renal function. When used in effective doses, ALDOMET usually does not reduce glomerular filtration rate, renal blood flow, or filtration fraction.

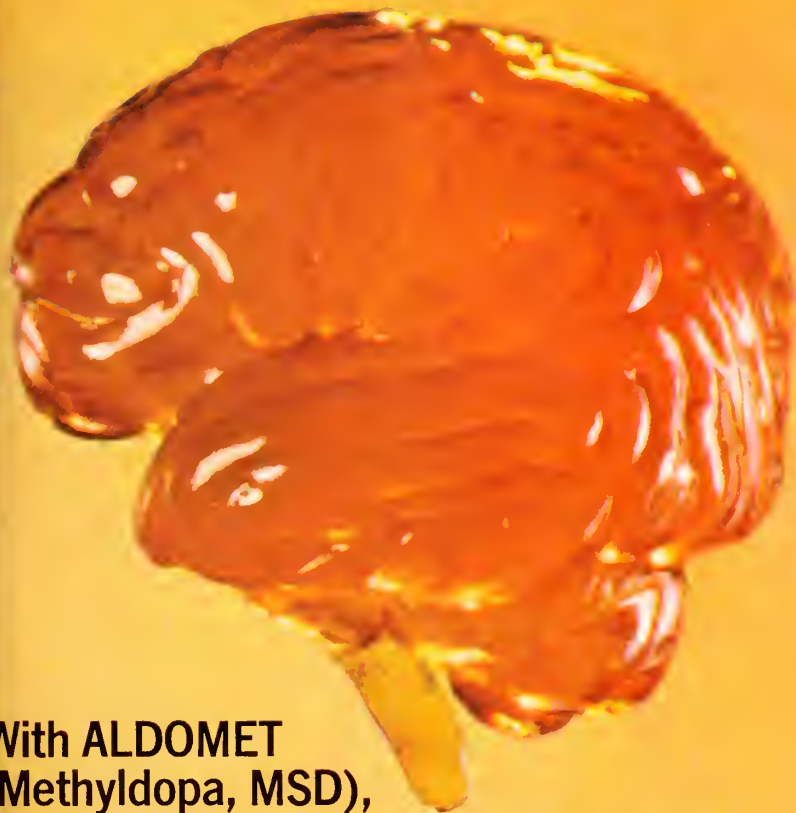


**With ALDOMET
(Methyldopa, MSD),
cardiac output is
generally unchanged**

ALDOMET has no direct effect on cardiac function. When ALDOMET is used in effective doses cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is slowed.

addendum

MSD
MERCK
SHARP
DOHME



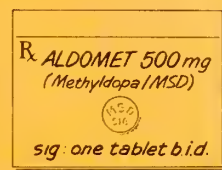
to further
simplify therapy
for many patients

now available
ALDOMET® 500mg
(METHYLDOPA | MSD)

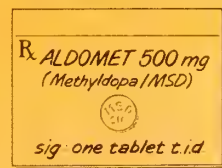
- often more practical to prescribe
- easier for patients to remember

Now offered in addition to the standard 250-mg tablet, the new ALDOMET 500 mg tablet is a patient convenience. An especially important one, since in hypertension convenience of the dosage schedule is one factor that can make the difference in compliance of the patient. The minimum daily dose of ALDOMET is 250 mg b.i.d. The usual starting dose is 250 mg t.i.d. Dosage is adjusted as necessary by adding or deleting 250 mg or 500 mg at intervals of not less than two days. The maximum dose is 3.0 g per day. Examples of b.i.d. or t.i.d. dosage convenience provided by ALDOMET 500 mg within the usual daily dosage range of 500 mg to 2.0 g:

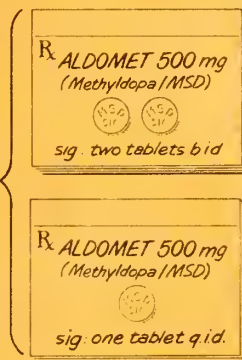
1.0-g
daily
dose =



1.5-g
daily
dose =



2.0-g
daily
dose =



NOTE: Tablets shown are not actual size.

With ALDOMET (Methyldopa, MSD), symptomatic postural hypotension is infrequent

ALDOMET reduces both supine and standing blood pressure. Less frequent symptomatic postural hypotension is experienced with ALDOMET than with many other antihypertensive agents. Exercise hypotension and diurnal blood pressure variations rarely occur.

for hypertension

TABLETS, 250 mg, 500 mg, and 125 mg

ALDOMET®

(METHYLDOPA | MSD)

a unique antihypertensive agent

ALDOMET is contraindicated in active hepatic disease, hypersensitivity to the drug, and if previous methyldopa therapy has been associated with liver disorders. It is not recommended in pheochromocytoma. It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

MSD
MERCK
SHARP
DOHME

For a brief summary of prescribing information, please see following page.

in hypertension

ALDOMET[®] (METHYLDOPA|MSD)

usually lowers blood pressure effectively



Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyl dopa therapy has been associated with liver disorders (see Warnings); hypersensitivity

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyl dopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyl dopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyl dopa. If a positive Coombs test develops during methyl dopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyl dopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyl dopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyl dopa, the drug should not be reinstituted. When methyl dopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyl dopa is stopped.

Should the need for transfusion arise in a patient receiving methyl dopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or

cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyl dopa. If caused by methyl dopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyl dopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Use in Pregnancy: Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyl dopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyl dopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyl dopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyl dopa because the drug is removed by this procedure.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression.

Cardiovascular: Bradycardia, aggravation of angina pectoris, orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyl dopa if edema progresses or signs of heart failure appear.)

Gastrointestinal: Nausea, vomiting, distention, constipation, flatulence, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

Hepatic: Abnormal liver function tests, jaundice, liver disorders.

Hematologic: Positive Coombs test, hemolytic anemia, leukopenia, granulocytopenia, thrombocytopenia.

Allergic: Drug-related fever, myocarditis.

Other: Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, dermatologic reactions including eczema and lichenoid eruptions, mild arthralgia, myalgia.

Note: Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third month of therapy. Increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

How Supplied: Tablets, containing 125 mg methyl dopa each, in bottles of 100; Tablets, containing 250 mg methyl dopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyl dopa each, in single-unit packages of 100 and bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

MSD MERCK SHARP & DOHME

FAMILY PLANNING IN SOUTH CAROLINA.

A Process of Growth and Development

KAREN M. LYNCH, M.A.*

J. E. PADGETT, JR., M.D., M.P.H.*

A dramatic change in thinking and practice regarding Family Planning has taken place in the past decade and a half in the United States. For example, it was only 1955 that a national magazine for the first time had an article that named specific contraceptives, and it was not until 1959 that a television network carried a program that mentioned the subject.

The shift in public policy can be said to have begun in 1958 in New York City. At that time, a campaign was initiated that reversed the ban on contraceptive prescriptions in the city's hospitals where the poor were treated.

Beginning in 1961, officials of the Kennedy Administration expressed concern over population growth and federal administrative policy began to shift after 1965 under pressure from Congress and President Johnson. The Department of Health, Education, and Welfare issued its first policy statement of family planning in 1966, but the first federal agency to move from words to action was the Office of Economic Opportunity which, as part of its antipoverty program, began to make grants to community action agencies in 1965 to finance voluntary family planning projects. In 1967, the Office of Economic Opportunity designated family planning for special emphasis in antipoverty programs while an amendment to the Social Security Act, also 1967, allocated at least six percent of federal funds appropriated for maternal and child health programs to be earmarked for family planning. In 1968, President Johnson appointed a family planning Committee and in 1969, President Nixon asked for increased support for the Family Planning Programs, which resulted in the

1970 Family Planning Services and Population Research Act. In 1971, the Department of Health, Education, and Welfare submitted to Congress a five year plan to provide family planning services to an estimated 6.6 million women by 1975. The change in public policy was thus expressed in numerous legislative and administrative actions at federal, state, and local levels. It was also expressed in the rapid expansion of organized family planning clinic programs serving persons of low or marginal incomes (from 150 in the United States in 1960 to 3,250 in 1975).

How did these changes in public policy affect South Carolina and how did South Carolina begin her involvement in Family Planning?

In July, 1938, a committee of the South Carolina Medical Association requested that the House of Delegates pass an enabling resolution so that the State Board of Health would be able to give contraceptive advice and materials to those under its care, who, in the opinion of a physician, were in need of it. In 1938, the resolution passed.

The first clinics were not called family planning and it was stressed that there would be no distinct "birth control" clinic, but that the supplies and advice would be given while the patient was in the general clinic for other services. The stated policy said, "The policy of the pregnancy spacing program is not a reduction of the population, but better babies and lower mortality for babies and mothers."

Earliest reports of family planning as a separate and distinct program appeared in 1964, and show approximately 1,700 patients enrolled. As of 1970, 17,165 were being reported as served. In 1971, 24,243 were reported as being served.

*Bureau of Maternal and Child Care, S. C. Dept. of Health and Environmental Control, Columbia, S. C.

FAMILY PLANNING IN S. C.

From 1939 to 1971, family planning was merely one of the services that county health departments were to offer. Very little, if any, publicity was given about family planning. It was not a program which received a high priority from state level operation of the State Board of Health. Some counties served as few as 50-60 people all year.

As previously stated, in 1965, the Office of Economic Opportunity began to make grants for family planning to their local Community Action Project agencies. The Office of Economic Opportunity operated family planning clinics in South Carolina in 28 counties through twelve projects. Ten of these projects were Office of Economic Opportunity funded but operated through health department clinics. The other two were funded by the Office of Economic Opportunity but operated in separate clinics by Planned Parenthood.

In addition to regularly operated health department clinics, joint Office of Economic Opportunity and health department clinics, and Planned Parenthood clinics, there were also some health department clinics operated as special Health, Education, and Welfare funded projects. Family planning was also provided by private physicians in their offices. In 1971, the Department of Health, Education, and Welfare became interested in trying to pull together all of the Family Planning Programs in each state into one umbrella program operation. South Carolina was one of the first states in the Southeast to attempt to pull all types of public family planning projects into one organization. This effort began in 1971, when South Carolina received funding from Title X of the Family Planning Services and Population Research Act of 1970.

The State Board of Health was chosen by the Department of Health, Education, and Welfare to be the lead agency in putting together the public family planning program in South Carolina. During FY 1971-72, the South Carolina Statewide Family Planning Program was created within the State Board of Health. That first year four district projects were funded. (South Carolina's 46 counties are divided into ten districts.) These districts had written plans specifying certain objectives to be accomplished. One main requirement of all district plans was that they specify how all the groups

were to offer family planning in a unified, comprehensive manner. The second year, FY 72-73, three additional district projects were begun and the third year, the remaining three. While these district projects were being organized, negotiations were ongoing to ensure coordination of effort. The end result was that, as of July 1, 1974, all family planning services in South Carolina supported by tax dollars through categorical grants were administered through the Statewide Family Planning Program, of the South Carolina Department of Health and Environmental Control. A single reporting system is used and all procedures are standardized.

The approach of South Carolina's Statewide Family Planning Program was built on many of the concepts generated by the Office of Economic Opportunity and health department programs. The use of community health aides to seek out potential patients and tell them about family planning was built into every district project. The basic premise was again that people, especially low income, will use family planning services if they know about them and if they are offered in a way that does not offend the patient's dignity. Other concepts such as patients serving on advisory boards to help decide on clinic locations, times, and program direction were implemented. Physician services in Family Planning clinics were provided by private physicians on a fee basis. By 1974, the state program had grown to the extent that some 56,000 women were participating in the Family Planning Program on a regular basis in South Carolina.

What are the concepts and approaches now? Most recent studies indicate that the fertility rate among the poor has declined more than that of the more affluent, but there is still a considerable way to go. Because of increased acceptance of clinic services by so many and the relative freedom of discussion of the subject of family planning (compared to early 1960's), it is believed that most people, rich and poor, have heard of family planning, birth control, infertility, the pill, etc. It is no longer sufficient to just send out the word about family planning. More emphasis must be put on improving the services in place now. New services such as male involvement and services to teens are essential. Use of nurse practi-

FAMILY PLANNING IN S. C.

tioners to provide service to patients without problems and keeping the patients involved who are already enrolled in Family Planning are becoming more important than searching for new patients. The Statewide Program loses about 25% or more of its patients every year. Too many of these losses result in unwanted pregnancies.

The concept now is not just provision of services, but provision in the most efficient and

effective manner. For example, we know from studies that for every dollar spent on family planning this year, more than \$2.00 will be saved by the government the very next year.

The South Carolina Statewide Family Planning Program has grown at a rapid rate in the four short years since its implementation. But, this has been just a beginning. There are still many areas for improvement and many questions to be answered. □

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The Pain Phone

When a telephone prescription for pain relief is necessary or convenient, you can call in your order for Empirin Compound with Codeine in 45 of the 50 states† That includes No. 4, which provides a full grain of codeine for more intense, acute pain.

†The exceptions:
Alaska, Arizona, Maine,
Oregon, Rhode Island, and
the District of Columbia

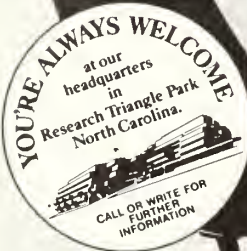
EMPIRIN[®] COMPOUND & CODEINE

No. 4 codeine phosphate*
(64.8 mg) gr 1

No. 3 codeine phosphate*
(32.4 mg) gr ½

Each tablet also contains aspirin
gr 3½, phenacetin gr 2½,
caffeine gr ½

*Warning—may be habit-forming.



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Research Triangle Park
North Carolina 27709

SCMA Executive Committee Meets with Pharmacists

Four representatives of the S. C. Pharmaceutical Association met with the SCMA Executive Committee on September 18 to establish a better rapport between the two associations.

Many worthwhile topics were discussed requiring action from both groups. Listed are those pertaining to physicians:

1. It was suggested that prescriptions written for Medicaid patients be based on the formulary in order that the patients may receive the medication and be reimbursed properly. The formulary is distributed to physicians periodically and updated. It is recommended that physicians refer to the formulary prior to writing prescriptions for patients who they know are on Medicaid. A joint effort between the two associations for co-payment was discussed along with an open formulary with cost control.

2. The pharmacists described difficulties they have experienced by physicians writing more than one prescription on a single blank. It is recommended that each prescription be written on a separate blank to avoid confusion and eventual problems to the patient.

3. Some physicians are permitting other people in their offices to phone in prescriptions. If this continues, it could have very serious legislative complications in the future. Discontinuing this will reduce the possibility of illegally obtaining drugs and there is less chance of error. The SCMA Executive Committee stated that it would much prefer that this be stopped on a voluntary basis; however, should the problem continue, SCMA may go on record as supporting legislation to prevent it. □

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MAKES SENSE

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® Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F) and 25 mg. of hydrochlorothiazide.

**TRIAMTERENE CONSERVES POTASSIUM
WHILE HYDROCHLOROTHIAZIDE
LOWERS BLOOD PRESSURE**

**FOR LONG-TERM CONTROL
OF HYPERTENSION***

Serum K⁺ and BUN should be checked periodically. (See Warnings Section.)



Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Warning

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Indications: *Edema* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has

been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and

BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

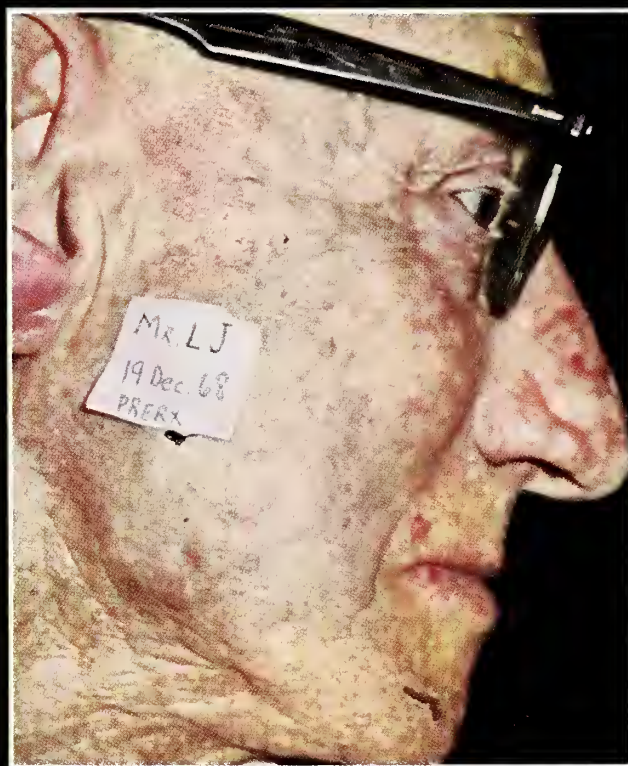
Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F Co., Carolina, P.R. 00630
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the sun and solar keratosis...

Overexposed



and often underdiagnosed

Solar keratosis is not an uncommon medical problem.

Of course, the prevalence of keratotic lesions is greater in locations south of the 38th parallel—the so-called "Solar Keratosis Belt"—receiving the greatest amounts of solar radiation. However, solar keratosis can occur among any light-skinned population, usually in persons over 40, wherever people are subject to extended exposure to the sun.

Solar keratoses are generally not difficult to identify.

These skin lesions are usually multiple, flat or slightly elevated, brownish or red in color, papular, dry, rough, adherent and sharply defined. They are found on areas of the skin having extensive exposure to sunlight. Clinical characteristics of the lesions, their predominant location on exposed surfaces, the age of the patient and his skin type are important considerations in the diagnosis.

Solar keratoses can, and should, be treated because they are potentially premalignant.

Chronic exposure to sunlight frequently leads to degenerative changes in the skin. This can often result in the development of multiple, potentially premalignant keratotic lesions. Therefore, early detection and treatment is advisable.

Treatment with Efudex (fluorouracil) provides a high degree of effectiveness with a low recurrence rate, ease and convenience of therapy, low incidence of scarring, excellent cosmetic results in most cases, and a high level of patient acceptability.

Efudex[®] 5% Cream fluorouracil/ Roche[®]

Because there may be more than meets the eye.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to

respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dis-

pensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris (hydroxymethyl) aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Case history for patient photographed at left on file, Hoffmann-La Roche Inc., Nutley, New Jersey.

TRAINING NURSES FOR CANCER DETECTION

Marian F. Keels, R.N.*

Paul H. O'Brien, M.D.**

Cancer detection currently requires the time and energy of busy clinicians. Clinicians properly concentrate their energies on high risk, more demanding professional challenges. It is not realistic to expect more widespread cancer detection examinations without providing new personnel. Such new people must expand and support the ongoing health care system.

We looked at the group available for training in this area. Our choice was the Registered Nurse. She is a responsible, recognized factor in health care. She has generally been taught to make decisions and act promptly in case of problems or emergency. She knows how to communicate with the physician and the patient.

Letters of intent were sent to physicians in the state of S.C. and their opinions requested. Nurses were nominated for this position. Four registered nurses were chosen for our first training session.

The first program was a week long and consisted of five eight-hour days. Anatomy of the anorectal area was reviewed. A film showing the actual sigmoidoscopic examination was shown. Printed material from text books and other available sources was sent to the nurse participants before their arrival for the course.

A Tutorendoscope and procto-trainer were purchased and used each afternoon during this

week. The Tutorendoscope is a machine through which slides of rectal and colon lesions can be viewed as if viewing the actual lesion through a sigmoidoscope. Another portion of the Tutorendoscope is a large viewing box on which the lesion can be seen in magnified proportion by several people at one time.

The procto-trainer is a unit on which insertion of the sigmoidoscope may be attempted before actual clinical practice. The nurses in our training program felt the Tutorendoscope was particularly helpful.

Dr. Leon Banov allowed these nurses to accompany him two mornings during the examination of his patients and taught them proper technique and psychological approach to the patient.

Surgical Residents in the Cancer Clinic at the Medical University were then utilized for assistance to aid the nurses in actually doing the proctosigmoidoscopic examination and again point out proper techniques. The patients had been treated originally for cancer other than in the colon area and were not routinely having this examination performed. (It should be noted here that during this time there were several abnormal findings and these patients referred to the proper area for treatment.) Each nurse participating in this program examined six patients in the presence of the surgical resident with a digital rectal exam with smear for occult blood on each patient.

At the end of this one week program, the participating nurses were confident they knew a proper technique and what the normal colon

*From the Medical University of South Carolina, Charleston, South Carolina.

**Director of the Cancer Clinic, Medical University of South Carolina, Charleston, South Carolina.

NURSES FOR CANCER DETECTION

should look like. The nurses were also taught how and what questions to ask the patient receiving this examination.

The participants in this program all worked for physicians in a family practice type setting. They are now allowed to perform a proctosigmoidoscopic examination on patients with a physician available.

We also tried two separate one-week programs teaching nurses to do pap smears and breast examinations. These programs were taught with the help of a member of the faculty from the MUSC College of Nursing-Nurse mid-wifery Program. There were four nurses trained in one week and six in another. Pelvic and breast manikins were used in a classroom as well as visual aids. The nurses were then allowed to do these examinations on patients from the local county hospital as well as in the cancer clinic under the supervision of the nurse midwife instructor.

Upon completion of this course, the nurse participants felt fully confident in techniques of taking a proper pap smear, digital rectal examination and breast examination as well as teaching the patient breast self examination.

The nurses in the pap-breast program worked: one in a physician office, another the

Women's Correctional Institute, an employee nurse for a S.C. hospital, and one in the area of public health.

The programs accomplished the goal that had been set and assured us that the nursing profession is the most appropriate area to draw assistants for the physician in early Cancer Detection.

Summary

Three separate one week courses were held for nurses in areas of cancer detection. The programs included instruction in taking of a proper pap smear, breast examination and proctosigmoidoscopy. The Tutorendoscope system was utilized for teaching proctosigmoidoscopy. Our nurses were all clever students who mastered with ease the diagnostic techniques used in cancer detection.

Acknowledgement

1. The Tutorendoscope System was invented and developed by H. David Markman, M.D., Associate Professor of Clinical Surgery at the Albert Einstein School of Medicine, New York, New York, and Visiting Associate Professor, Dept. of Surgery, New York Medical College.

2. Funds for this project were provided by the South Carolina Regional Medical Program.

REFERENCES

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The AAPS Annual Meeting in Disney World, October, 1975

Perhaps the most important happening there was the election of Dr. F. M. Ball of Charleston as President-Elect. He will take office, God willing, in October of 1976. It is a wonderful thing to see God replacing old leaders with new, and to note the improvement in quality.

Everybody had a good time. Happy reunions with old friends are always enjoyable. Accommodations were excellent, the entertainment decent, the prices were remarkably reasonable, and the speakers, as always, excellent and understandable.

President Frank Rogers discussed what doctors can do to save liberty. Briefly, we must study to understand our rights, and we must defend them ourselves, not looking to some third party or union to do it for us.

James Stewart Cox, a lawyer from Memphis, told us how to avoid the pitfalls of malpractice lawsuits. First of all, we must establish good personal relations with our patients, so that they will know we value them as individuals and as friends, and that we intend to act in their best interest to the utmost of our ability. Then, if something goes wrong, while telling the truth in speech and writing, we must avoid putting derogatory remarks about ourselves or others into the record. By no means must we reduce charges or offer to pay the patient's bill, for we have acted in good faith; and we must keep both patient and family informed as to what is going on. Many lawsuits are based upon too great expectations, misunderstandings, or hurt feelings: so by all means treat your patients with candor and kindness. Mr. Cox

expressed the further opinion that arbitration procedures, though useful, could not prevent subsequent recourse to the courts by dissatisfied patients. He further opined that there was no fool-proof legal remedy because most proposed laws would turn out to be class legislation and therefore unconstitutional. AAPS has a committee which has this matter under continuing study.

W. Philip Gramm, Ph.D., Prof. of Economics at Texas A & M, explained that the cause of unemployment and inflation is not the result of profligate spending by our citizens but by our government, which finances its excesses by printing unbacked paper currency, thus making matters continually worse. Since Congress authorizes this folly, Congress can also end it by returning to fiscal sanity and a balanced budget; and it is up to our citizens to force Congress to do its duty, by electing men who will think of their country's long-term welfare instead of their own immediate interests.

Dr. P. A. T. Wood of Suffolk, England, related how he and 500 other physicians had survived in the practice of private medicine in Britain. It is inspiring to meet heroes, especially happy articulate heroes.

And that's not all. But if you want to know what else goes on at AAPS meetings, and who is there, you had better come to see. The interim meeting will be in Chicago April 23-24, 1976; the next annual meeting will be at the Camelback Inn, Scottsdale, Arizona, Oct. 21-23, 1976

Thomas Parker, M.D.

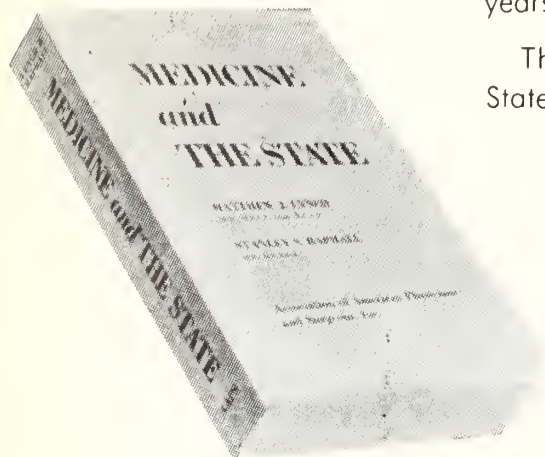


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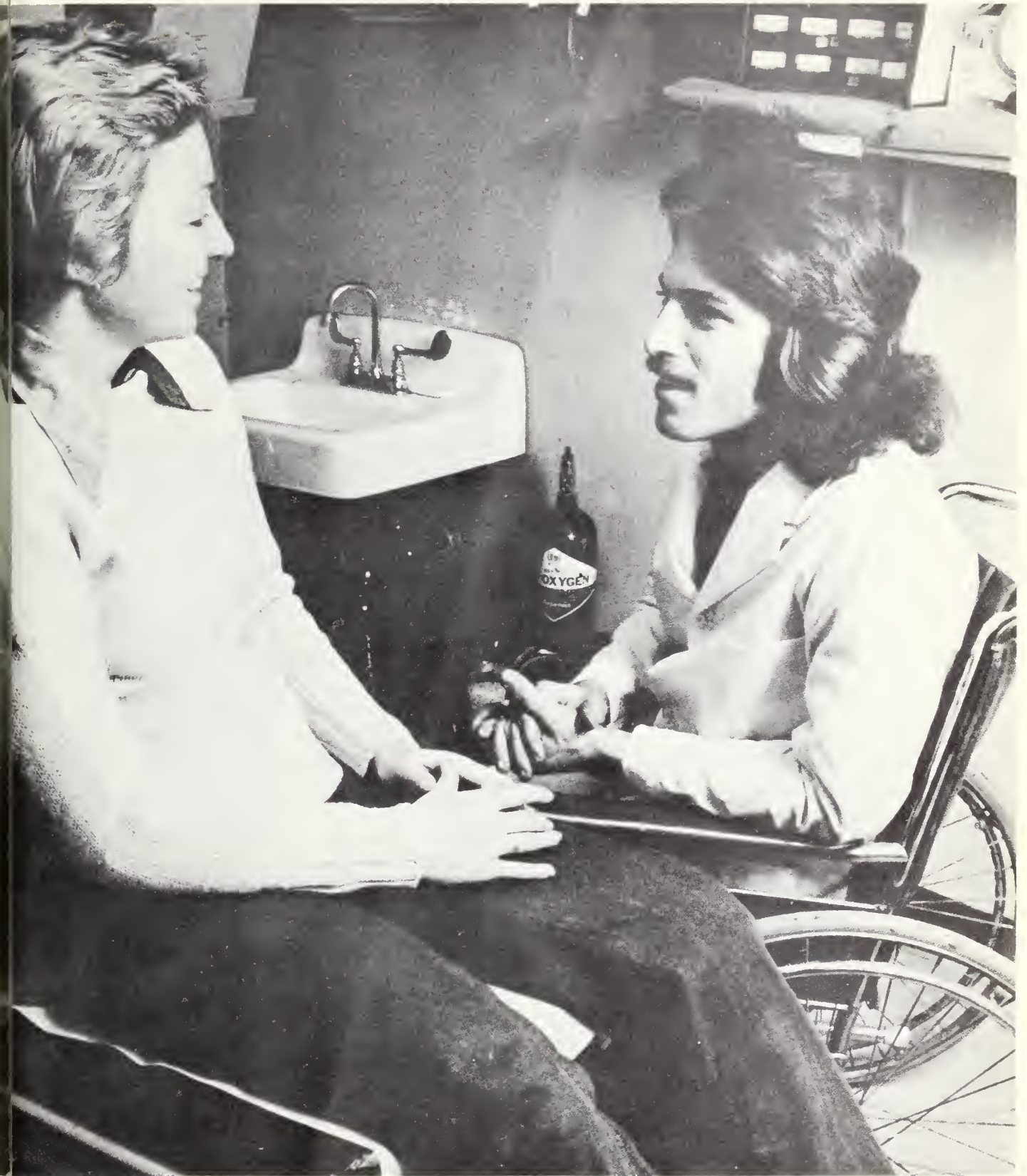
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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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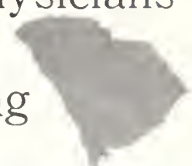
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ADVERSE REACTIONS: Drowsiness, fatigue, vertigo, incoordination, tremor, muscle weakness, ataxia, hypotension, respiratory depression, delirium and coma. Dryness of nose, mouth, and throat, pupillary dilatation or blurred vision, urinary retention, abdominal pain, nausea, vomiting, diarrhea, and hypersensitivity reactions. Overdose may result in hallucinations, excitement, ataxia, incoordination, athetosis, convulsions, and death.

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Treatment. Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonists naloxone, nalorphine or levallorphan are specific antidotes against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including oxycodone. Therefore, an appropriate dose of one of these antagonists should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric emptying may be useful in removing unabsorbed drug.

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THE MEASUREMENT OF ENERGIES OF LIFE PROCESSES

GILBERT B. BRADHAM, M. D.*

This article is presented simply to acquaint South Carolina medicine with a unique means of attaining specific basic medical information. For the past several years we have developed progressive methods of measuring the energy required to operate living processes. These efforts have culminated in a current method of measuring the energies required by the in-hospital patient during a course of serious illness. While these measurements have generally concerned the surgical patient, they have also been used to study states of metabolism during other illnesses and have lately involved the children of the pediatric wards.

The measurement of the energies required for the process of maintaining life is not by any means a new inquiry. Laplace and Lavoisier developed one of the first calorimeters for animal use and established the role of oxidation in the production of body heat.¹ Our reasons for redeveloping interest in this area was to inquire as to the reliability of interpreting energy requirements during serious surgical illnesses. Additionally, it would appear that changes in energy requirements might allow observation of subtle changes in health not feasible by other means.

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Methods

During the past six to eight years, a laboratory has been developed which has focused its attention upon the measurement of the energies evolved from the processes of life. In this laboratory have been tested all of the previous methods of measurement of energy from living processes. These methods have been applied to mice, larger laboratory animals, and to man. Two methods have remained from this study and are currently used.

Indirect Calorimetry: Indirect calorimetry is a measurement both of the oxygen absorbed by the living process and the carbon dioxide evolved in the same process. The ratio of the oxygen consumed to the carbon dioxide evolved is termed the respiratory quotient and is typical of the fuel which supplies the energy needed for the life process. Since the energy equivalents of body fuels are known, the actual quantity of energy being used by the living process is proportional to the quantity of oxygen consumed.

Direct Calorimetry: Direct calorimetry is a direct measurement of energy as it is transferred from the life process to the environment. This transfer occurs by several methods. Thermal energy evolving from chemical reactions occurring in the body can be radiated (skin, as

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Fig. 1

an example, is a near perfect radiator), lost by convective currents, or directly conducted to the surroundings. Thermal energy is also lost to a significant degree by evaporation. It is required that 576 gram-calories are used to vaporize one gram of water at 37°C.² The human, losing one liter of water by evaporation, thus transfers 576 kilocalories to the environment by having changed liquid water to water vapor.

Radiated, convected and conducted energies are currently best measured by a gradient layer calorimeter which has been developed to accommodate human patients.³ The calorimeter is a chamber measuring 8 feet in length, 3 feet in width, and 3 feet in height (Figure 1). It is supported on a stand which is mobile. The walls of the calorimeter are constructed in the following manner: The inside walls are constructed of panels containing 74,000 thermocouples which are connected in series. These thermocouples are arranged in pairs which are separated by a very thin layer of plastic material. Arranged in this manner, the pairs of thermocouples form a gradient layer capable of measuring the difference in temperature across a thin layer of space. Since they are connected in series, the total electrical signal which they generate is proportional to the difference in the total quantity of heat which they separate. On the outside of the thermocouple layer is an aluminum shell. Mounted against the outer wall of the aluminum shell is a series of copper pipes arranged to keep the aluminum shell at constant temperature by means of circulating water at constant temperature. The copper pipes are within a layer of foam insulation. Covering the insulation is a metal heat shield which forms the exterior of the calorimeter.

At one end of the calorimeter is a door constructed in the same manner as the walls of the calorimeter. The door is arranged to close as a hermetic seal. At the opposite end of the calorimeter is a large window. The window is formed of a layer of polycarbonate acrylic, a dead airspace, a glass enclosure of freon, another dead airspace, and a final layer of polycarbonate acrylic. The structure of the window permits easy visualization of the interior of the calorimeter, but permits less than 0.05 per cent of its heat loss.

On the floor of the calorimeter are tracks on which a mobile stretcher rides which is easily removable for cleaning and sterilization.

The electrical output of the calorimeter is connected to a suitable recorder. The recorder is capable of displaying the quantity of heat being lost by the patient at any instant, of producing a graph of the heat loss, of adding all of the heat lost, and providing a printed record. The calorimeter has electrical connections to the interior to provide electrocardiographic recording, blood pressure recording, or any other suitable monitor. Mounted on the stretcher is a microphone system, which allows two way conversation to the outside without the necessity of manual control. There are two large ports through which air flows into and out of the calorimeter. The temperature of the airflow is controlled by electric heaters. The air heaters are controlled by linear quartz thermometers which measure temperature to 0.0001 of a centigrade degree. By this means, there is no net convective heat loss by the patient even though he is constantly bathed with room air of a desired temperature.

Humidity of the interior of the calorimeter is monitored and kept at approximately 30 per cent relative humidity. Carbon dioxide is monitored by an infrared carbon dioxide analyzer. Oxygen can be monitored by a Pauling paramagnetic oxygen analyzer.

The patient is weighed on a metabolic scale placed in the calorimeter. This scale is accurate to 1 gm. The patient is rolled into the calorimeter on the stretcher and is monitored for the desired time. During this period of time, the patient is totally unconstrained and is essentially as comfortable as being in his bed.

Water vaporization is generally measured by a change in weight of the subject over a period of time. Currently such a change in

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weight is measured by a modified Brookline Metabolic Scale as mentioned above.

Finally, it should be mentioned that energy is transferred to the environment as a change in the chemical structure of materials ingested and wasted. These latter energies are small relative to those already discussed and are generally regarded only in the highly critical context of physiological research.

Results

Initially it was of interest to us to have knowledge of the quantity of immediately transferable energy contained by the mammalian body. By immersion of mice into liquid nitrogen, the process of metabolism could be immediately stopped. If this process were done atop a sensitive scale, the vaporization of the liquid nitrogen caused by the transfer of all available thermal energy (down to the temperature of the nitrogen) could be reliably measured. With knowledge of the heat of vaporization of liquid nitrogen, the actual specific thermal capacity of whole living animals was established at 0.85.⁴

It was one of the original theses of this project that living processes would respond to stressful events by harnessing available energy to confront the stress. In cases, it might be that the mechanics of use of this energy would be insufficient in this confrontation. In either

event, the organism could be viewed as either being stable in his use of energy in the successful process of living or significantly unstable when failing in this process. These relative states of stability could be objectively viewed through a comparison of energy available by indirect calorimetry and energy transferred to the environment by measurement using direct calorimetry.⁵

Table 1 depicts the results attained in the measurement of normal subjects, and shows that normal healthy adult subjects generate approximately 32 kilocalories for every kilogram of body weight during each day. In contrast, the hyperthyroid patient generates approximately 40 kilocalories per kilogram per day. The thermally burned patient (Table 2) may generate 45 kilocalories per kilogram per day. Moreover, in the hypermetabolic states, evaporation dominates as the method by which the body best loses its excessive energies.⁶

Measurements on the morbidly obese patient have been most consistent. When their needs are expressed in terms of kilocalories per kilogram body weight per day, the average result (17 K-cal/Kg/d) appears low. Although the figure as expressed in terms of kilocalories per kilogram body weight/day appears low, multiplying the patient's excessive weight by this figure reveals that all morbidly obese pa-

Table 1. Energy Losses of Normal Volunteers.

No.	Total Kilocalories Kg day	% due to Radiation	% due to Evaporation
1	23.5	66	34
2	33.8	84	16
3	29.6	69	31
4	32.1	63	37
5	33.0	81	19
6	39.5	80	20
7	28.7	70	30
8	37.5	60	40
9	35.7	61	39
10	34.0	63	37
11	28.6	78	22
12	26.5	71	29
Average	31.9	70%	30%

These are the rates of energy loss from healthy young men and women. The average figure of approximately 32 kilocalories per kilogram of body weight per day would mean that a 70 Kg. person would require 2240 kilocalories

per day to perform resting functions. Approximately 30% of this energy is lost by evaporation, the remainder by other means (see text).

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Table 2. Initial Energy Losses of Eight Burned Patients.

Patients	Kilocalories Kg/day	% Radiation	% Evaporation
1	46.3	45	55
2	88.4	26	74
3	35.7	79	21
4	33.6	63	37
5	28.9	75	25
6	26.9	71	29
7	32.3	64	36
8	67.1	27	73
Average	44.9	56	44

This table depicts the increased rates of metabolism of burned patients. It also shows that the burned patient

loses a greater proportion of his energies by evaporation than does the normal person.

tients studied to date require energy in excess of their less weighty counterparts (Table 3).

We have also now had the opportunity to study the young, and on occasion, the older patient and the moribund patient. The results of studies in some pediatric conditions are summarized in Table 4 to show the extremely high requirements of children and the proportion to age of these requirements.

Comment

These results have been arranged to give a portrait of research interest rather than to establish in a highly specific manner some new scientific datum. They begin by showing new methodology in establishing for the first time a correct term for total body heat content. Moreover, by extracting in an almost immediate sense the energy required for life in the mice experiments, it was noted that no large bursts of energy became available to attest to the availability of long conjectured energies of living organization. These are new data and proofs of scientific concepts.

The dog experiments established the prin-

ciple of instability as existent in living organisms during stress. From a thermodynamic sense, the unstable state is one not only of wastage of available energy, but also one requiring energy in excess of usual demands to attain again the stable state of health. Moreover, these measurements allow a critically objective method of viewing the stability of living processes without invasion of their living domain.

The patient studies are a variety of interests in particular states of illness as they relate to the patients energy requirements. The normal studies were done upon volunteer medical students, residents, nurses and secretaries, all young adults in excellent health. The values attained are remarkably closely grouped, showing that young healthy adults require similar quantities of energy. These studies were carried out at complete rest and reflect "resting metabolism" or that quantity of energy flow required simply "to keep body and soul together." At this ideal state the body is like a giant candle to which tallow is being added at

Table 3. Energy Requirements in Four Obese Patients.

Patients	Kilocalories Kg/day	Kg body weight	Total Kilocalories per day
1	16.4	140	2296
2	15.2	110	1672
3	16.4	117	1918
4	22.7	173	3927
Average	17.67	135	2385

Obesity gives the initial appearance of low metabolism if viewed on a per kilogram body weight basis. When mul-

tiplied by the patients actual weight the true state of normal to excessive energy needs are noted.

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Table 4. Energy Requirements of Pediatric Patients.

Patients	Age	Cal/Kg/d	Radiative	Evaporative
1	4 mos.	184	82%	18%
2	11 mos.	102	69%	31%
3	16 mos.	133	71%	29%
4	4 yrs.	96	71%	29%
5	4 yrs.	81	78%	22%
6	5 yrs.	85	74%	26%
7	6 yrs.	86	---	---
8	11 yrs.	42	82%	18%

Children require more energy per unit weight than do adults. This is particularly evident at the ages of infancy. As explained in the text, these energy requirements be-

come most significant during illnesses which disallow the replacement of energy at the same rate at which it is lost.

the same rate at which it burns. It neither does work nor does it change in any way. At this state the oxygen consumed as fuel "burns" and is directly proportional to the energy transferred to the environment, for the flame and the fuel supply are steady. Since no energy is used to perform work upon either the environment or upon the body itself, all energies liberated in the oxidative reactions sink into the environment. The body is at a relatively steady state with respect to both mass and energy. An abnormal physiological state, such as hyperthyroidism, is reflected as a hypermetabolic state from an energetic view. The wheels in the machine turn faster. It is probable that the machine is less efficient but that point is difficult to prove. If the patient can provide himself with food equal to the rate of his increased metabolic rate, then he need not lose weight as is typical, but rather on rare occasion can actually ingest more than is needed, and gain weight. This patient nonetheless is radiating energy at a more rapid rate than normal and also evaporating more water. The weight of hyperthyroid patients changes a great deal more precipitously than it does in the normal patient.

The thermally burned patients have provided us with much interest. First, they are all hypermetabolic (which is the reason for their characteristic weight loss), and, secondly, we have learned to recognize that they dissipate their excessive energies primarily through the route of evaporation. The two points are both clinically oriented. The burned patient should be fed high caloric diets simply to supply his energy needs. Secondly, his physician should

be aware that the burn injury has partially destroyed the barriers to evaporation and this process now becomes a dominating factor in transfer of energy from the patient to the environment. Burned patients may become dehydrated, hypothermic, or chronically depleted of their energy stores by the process of excessive water vaporization at the burn site.

Morbidly obese patients have been of interest to our studies. When the energy requirements of fat people are viewed in terms of kilocalories per kilogram body weight per day, the figure appears small. It must be remembered that each kilogram of a fat person represents a higher proportion of fat than is normal. These are tissues of low metabolism. When the rate of metabolism of fat people is multiplied by their total weight it is always found that they are requiring of relatively large amounts of energy each day. We have found no fat people who do not eat, surreptitiously or otherwise, more food than the average nonfat person. The fat person eats too much. It is improbable that his gut is any more efficient than the average gut in the absorption of foodstuffs. It is highly probable that the fatter he gets, the less physical activity he performs, thereby compounding his problem. In this way fat people get fatter, thin people stay thin.

The very young person is interesting from an energetic view. The highest rates of metabolism are at birth, thereafter diminishing rapidly to puberty, taking a brief rise and then settling to fair stability until middle age at which they progressively decline. The extremely high rates of metabolism in young

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children keep the physician aware of the same necessities as in the burned or septic patient. The young child must be guarded during an illness against rapid dehydration, hypothermia, and depletion of available energy.

Conversely, the elderly patient with a generally decreased rate of metabolism must be guarded against over-empulsive ministrations of food and water, particularly the latter. It has been our experience to observe that the inexperienced physician will generally overhydrate his geriatric patients, causing more instances of pulmonary edema than of dehydration.

Finally, the preterminal cancer patient has been observed energetically on a few occasions. While our data is insufficient to allow conjecture, it does appear that this group of patients deserves study. We are beginning to view neoplasia as similar to new normal growth. It may be that the lack of control and differences in morphology and function of neoplasia are the effects of attempting to equilibrate with an altered energy supply.

Conclusion

The study of the flow of energy through liv-

ing processes is being studied at the Medical University in laboratory animals and in human patients. Such study has allowed the provision of new data basic to a more specific description of living processes and it has allowed an interesting view of clinical conditions. In the latter instance, health is defined as a state when the body is so well construed that the energy flow through it is steady. During illness the living process becomes unstable and may require care and thoughtfulness on the part of the physician to allow a return to the balanced state of health.

These considerations are not only made uniquely at different phases of the life process but they also require appreciation of the modes of normal and abnormal energy dissipation.

Acknowledgement

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WARNINGS: TRIAVIL should not be given with guanethidine or similarly acting compounds. Use cautiously in patients with history of urinary retention, angle-closure glaucoma, increased intraocular pressure, or convulsive disorders. In patients with angle-closure glaucoma, even average doses may precipitate an attack. Patients with cardiovascular disorders should be watched closely. Tricyclic antidepressants, including amitriptyline HCl, particularly in high doses, have been reported to produce arrhythmias, sinus tachycardia, and prolongation of conduction time. Myocardial infarction and stroke have been reported with tricyclic antidepressant drugs. Close supervision is required for hyperthyroid patients or those receiving thyroid medication. Caution patients performing hazardous tasks, such as operating machinery or driving motor vehicles, that drug may impair mental and/or physical abilities. Not recommended in children or during pregnancy.

PRECAUTIONS: Suicide is a possibility in depressed patients and may remain until significant remission occurs. Such patients should not have access to large quantities of this drug.

Perphenazine: Should not be used indiscriminately. Use with caution in patients who have previously exhibited severe adverse reactions to other phenothiazines. Likelihood of untoward actions is greater with high doses. Closely supervise with any dosage. The antiemetic effect of perphenazine may obscure signs of toxicity due to overdosage of other drugs or make more difficult the diagnosis of disorders such as brain tumor or intestinal obstruction. A significant, not otherwise explained, rise in body temperature may suggest individual intolerance to perphenazine, in which case discontinue.

If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perphenazine. Phenothiazines may potentiate the action of central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol) and atropine. In concurrent therapy with any of these, TRIAVIL should be given in reduced dosage. May also potentiate the action of heat and phosphorus insecticides.

Amitriptyline: In manic-depressive psychosis, depressed patients may experience a shift toward the manic phase if they are treated with an antidepressant. Patients with paranoid symptomatology may have an exaggeration of such symptoms. The tranquilizing effect of TRIAVIL seems to reduce the likelihood of this effect. When amitriptyline HCl is given with anticholinergic agents or sympathomimetic drugs, including epinephrine combined with local anesthetics, close supervision and careful adjustment of dosages are required.

Caution is advised if patients receive large doses of ethchlorvynol concurrently. Transient delirium has been reported in patients who were treated with 1 g of ethchlorvynol and 75-150 mg of amitriptyline HCl.

Amitriptyline HCl may enhance the response to alcohol and the effects of barbiturates and other CNS depressants.

Concurrent administration of amitriptyline HCl and electroshock therapy may increase the hazards associated with such therapy.

Such treatment should be limited to patients for whom it is essential. Discontinue several days before elective surgery if possible. Elevation and lowering of blood sugar levels have both been reported.

ADVERSE REACTIONS: Similar to those reported with either constituent alone.

Perphenazine: Side effects may be any of those reported with phenothiazine drugs: extrapyramidal symptoms (opisthotonus, oculogyric crisis, hyperreflexia, dystonia, akathisia, acute dyskinesia, ataxia, parkinsonism) can usually be controlled by the concomitant use of effective antiparkinsonian drugs and/or by reduction in dosage, but sometimes persist after discontinuation of the phenothiazine.

Tardive dyskinesia may appear in some patients on long-term therapy or may occur after drug therapy with phenothiazines and related agents has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. Symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth, or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Involuntary movements of the extremities sometimes occur. There is no known treatment for tardive dyskinesia; antiparkinsonism agents usually do not alleviate the symptoms. It is advised that all antipsychotic agents be discontinued if the above symptoms appear. If treatment is reinstituted, or dosage of the particular drug increased, or another drug substituted, the syndrome may be masked. It has been suggested that fine vermicular movements of the tongue may be an early sign of the syndrome, and that the full-blown syndrome may not develop if medication is stopped when lingual vermiculation appears.

Other side effects are skin disorders (photosensitivity, itching, erythema, urticaria, eczema, up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; hyperglycemia; endocrine disturbances (lactation, galactorrhea, gynecomastia, disturbances of menstrual cycle); altered cerebrospinal fluid proteins; paradoxical excitement; hypertension; hypotension, tachycardia, and ECG abnormalities (quinidine-like effect); reactivation of psychotic processes; catatonic-like states; autonomic reactions, such as dry mouth or salivation, headache, anorexia, nausea, vomiting, constipation, obstipation, urinary frequency or incontinence, blurred vision, nasal congestion, and a change in pulse rate; hypnotic effects; pigmentary retinopathy; corneal and lenticular pigmentation; occasional lassitude, muscle weakness, mild insomnia. Other adverse reactions reported with various phenothiazine compounds include blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia); liver damage (jaundice, biliary stasis); grand mal convulsions; cerebral edema; polyphagia; photophobia; skin pigmentation; and failure of ejaculation.

Amitriptyline: Note: Listing includes a few reactions not reported for this drug, but which have occurred with other pharmacologically similar tricyclic antidepressant drugs. **Cardiovascular:** Hypotension, hypertension, tachycardia, palpitation; myocardial infarction; arrhythmias; heart block; stroke. **CNS and Neuromuscular:** Confusional states; disturbed concentration; disorientation; delusions; hallucinations; excitement; anxiety; restlessness; insomnia, nightmares; numbness, tingling, and paresthesias of the extremities; peripheral neuropathy; incoordination; ataxia; tremors; seizures; alteration in EEG patterns; extrapyramidal symptoms; tinnitus; syndrome of inappropriate ADH (antidiuretic hormone) secretion. **Anticholinergic:** Dry mouth; blurred vision; disturbance of accommodation; constipation, paralytic ileus; urinary retention; dilatation of urinary tract. **Allergic:** Skin rash; urticaria; photosensitization; edema of face and tongue. **Hematologic:** Bone marrow depression including agranulocytosis, leukopenia; eosinophilia; purpura; thrombocytopenia. **Gastrointestinal:** Nausea; epigastric distress; vomiting; anorexia; stomatitis; peculiar taste; diarrhea; parotid swelling; black tongue. **Endocrine:** Testicular swelling and gynecomastia in the male; breast enlargement and galactorrhea in the female; increased or decreased libido; elevated or lowered blood sugar levels. **Other:** Dizziness; weakness; fatigue; headache; weight gain or loss; increased perspiration; urinary frequency; mydriasis; drowsiness; jaundice; alopecia. **Withdrawal Symptoms:** Abrupt cessation after prolonged administration may produce nausea, headache, and malaise. These are not indicative of addiction.

OVERDOSAGE: All patients suspected of having taken an overdosage should be admitted to a hospital as soon as possible. Treatment is symptomatic and supportive. However, the intravenous administration of 1-3 mg of physostigmine salicylate is reported to reverse the symptoms of tricyclic antidepressant poisoning. Because physostigmine is rapidly metabolized, the dosage of physostigmine should be repeated as required particularly if life-threatening signs such as arrhythmias, convulsions, and deep coma recur or persist after the initial dosage of physostigmine. On this basis, in severe overdosage with perphenazine-amitriptyline combinations, symptomatic treatment of central anticholinergic effects with physostigmine salicylate should be considered.

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CHRONIC INTUSSUSCEPTION OF MECKEL'S DIVERTICULUM

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E. EUGENE JONES, M.D.**

This report concerns the diagnosis of a Meckel's diverticulum in a patient referred for chronic anemia. A brief discussion of the complications arising from this anomaly is presented and newer radiographic techniques in diagnosis are reviewed.

Case History

A 17-year-old caucasian male was admitted for evaluation of chronic anemia. He had complained of malaise and had experienced intermittent, cramping epigastric pain for several months. A documented weight loss of ten pounds had also occurred during this time. On initial physical examination, the vital signs were normal. HEENT exam as well as chest and cardiovascular exams were also normal. The abdomen was scaphoid, soft and non-tender. No organomegaly or masses were present. Bowel sounds revealed normal peristalsis. There was no abnormal lymphadenopathy. Rectal exam and procto-sigmoidoscopy were normal. A stool guaiac was positive for occult blood.

The patient's initial hemoglobin was 3.6 grams and red cell indices revealed a microcytic, hypochromic anemia. Serum iron was 38 mcg%. A barium enema was negative. An upper gastrointestinal series demonstrated a small hiatus hernia and jejunal diverticulum. A small bowel series was performed which showed a possible defect in the distal ileum consistent with a Meckel's diverticulum (Fig. 1). Mesenteric arteriograms confirmed the presence of abnormal vasculature in this area (Fig. 2).

At laparotomy, a chronically intussuscepted Meckel's diverticulum was found and resected. The patient had an uneventful postoperative course and was discharged on the tenth postoperative day.

Pathological Examination

The pathological specimen consisted of a segment of distal ileum containing an inverted polypoid mass consistent with an inverted Meckel's diverticulum. Microscopic examina-

tion showed extensive interstitial hemorrhage and necrosis. No evidence of ectopic gastric or pancreatic tissue was found. Comment: Presumably this patient's chronic anemia was secondary to the necrosis and hemorrhage at the tip of the specimen (Fig. 3).

Discussion

The problems in diagnosis of a Meckel's diverticulum have long been appreciated by clinicians. This is largely due to the fact that complications related to a Meckel's diverticulum can present in many different ways.⁹



Fig. 1. Small bowel series demonstrating an intra-luminal mass in the distal ileum partially coated with contrast material.

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Fig. 2. Superior mesenteric arteriogram showing abnormal vasculature in the region of the distal ileum.

Bleeding, obstruction, infection, perforation, or combinations of these problems represent the most frequently encountered complications.^{3, 12} Additionally, the anatomical location of this anomaly has made diagnosis difficult by ordinary radiographic techniques.⁴ As a result, the correct diagnosis is frequently made late in the course of a patient's illness and consequently morbidity is high.¹⁰

Bleeding from the rectum caused by a Meckel's diverticulum may be massive or chronic.¹¹ In a series by Berman and Schneider, 50 per cent of their patients with Meckel's diverticulum contained ectopic gastric mucosa and this value increases to 90 per cent when bleeding or perforation was the chief symptom.²

Obstruction is usually the second most common mode of presentation. In a 25-year review of symptomatic patients with Meckel's diverticulum, 26 patients presented with intestinal obstruction.¹¹ In these patients, the obstruction was due to volvulus about a vitello-umbilical cord or about a mesodiverticular band. These authors distinguish the mesodiverticular

bands from solitary adhesive bands by the presence of a distinct course and vascular component.

Intussusception is another mechanism of obstruction. The intussusception may be ileo-colic or ileo-ileal. In some patients lymphoid hyperplasia or mesenteric adenitis were prominent findings suggesting they may have played a role in the pathologic process.¹ Other well-documented causes of obstruction include Littre's hernia, and obstruction secondary to localized inflammation, but these are much less common.

Infection arising in a Meckel's diverticulum may be related to abundant amounts of hyperplastic lymphoid tissue or ectopic pancreatic or gastric tissue.⁵ Occasionally, enteroliths form in the diverticulum and give rise to chronic obstruction. Perforation is usually secondary to advanced infection but may be secondary to ingestion of sharp objects.⁸

Recent technological advances in radiology may improve the accuracy of diagnosis in this disease. Angiographic demonstration of the site of gastrointestinal bleeding, as well as radio-isotopic scans offer hope to the clinician faced with the problems of obscure lower GI bleeding.^{6, 7} Tc^{99m}Na pertechnetate has been used to demonstrate Meckel's diverticulum containing ectopic gastric mucosa. But however helpful these new adjunctive methods may be, the clinician must continue to rely on a careful history and a high "index of suspicion" when faced with the diagnosis of abdominal disease caused by a Meckel's diverticulum. □



Fig. 3. Pathological specimen showing inverted diverticulum with hemorrhage and necrosis of tip.

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LOXOSCELISM

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Loxoscelism is the medical disorder caused by envenomization during the bite of the brown recluse spider, *Loxosceles reclusa*. This entity has only been recognized during the past 18 years; reports in the medical literature were almost nonexistent earlier. The characteristic bite was first attributed to the recluse spider in 1957 by Atkins.¹ Since this report, approximately 70 case reports have been recorded in the medical literature. The brown recluse spider inhabits a large geographical area consisting of the Southern central states. Recently we reported ten envenomizations by the recluse spider to have occurred in South Carolina.² The geographical range, we believe, has not increased for this spider. The bite is now more commonly recognized as a specific clinical entity and is being correctly identified, instead of placed in the category of "insect bite."

From a clinical viewpoint, the spider has caused uncommon, yet serious, clinical problems by its bite. In the United States, the bite of the black widow spider (*Latrodectus mactans*) and brown recluse spider (*Loxosceles reclusa*) probably account for most of the reported cases of spider bites. Russell³ stated that perhaps there are 50 species of spiders in the United States which have been implicated in bites on human beings. Recently we added to the list by reporting a rare bite by the spider *Herpyllus Ecclesiasticus* in South Carolina.⁴ A careful history and an attempt at spider identification are mandatory in cases of suspected spider bites.

The clinical presentation of the brown spider bite has varying symptomatology, depending upon the amount of venom injected

and the age and general health of the patient. The spectrum of reactions may vary from a very minor temporary irritation to a full-blown severe reaction with severe pain. The severe systemic response, which occasionally occurs, can cause death. The lesion produced by the brown spider bite is quite typical and quickly alerts one's suspicion to consider arachnidism. Aver and Hershey⁵ have classified the clinical appearance of the spider bite into four groups based upon increasing severity. The first group appears with only local itching without systemic signs. The second group presents as a local vesicle with an area of necrosis less than one cm. in size. The third group has an area of necrosis greater than one cm. in size and shows mild to moderate toxic systemic signs. The last group has an area of necrosis of greater than four cm. which is occasionally secondarily infected. These patients have definite systemic symptoms such as severe hemolysis, high fever, hemoglobulinuria, disseminated intravascular coagulopathy, occasion renal failure and, possibly, shock.

Some generalizations are possible concerning the symptomatology and clinical course following a brown spider bite. A stinging sensation usually occurs at the time of the bite. The bite can be relatively painless and may go unnoticed at the time of envenomization. In approximately half of the reported cases, the presenting lesion is on the buttocks, upper thigh, or foot. Unfortunately, the spider is infrequently caught and retrieved for precise identification. During the first eight hours following the bite, local pain is usually the only symptom. A particular characteristic of the *Loxosceles* bite is a blue-gray colored vasoconstrictive halo which spreads around the spider puncture site. After 12 to 18 hours, a small bleb develops at the site which is accompanied

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by a surrounding zone of erythema and edema. The bleb soon ruptures and a thin crust replaces it. The erythema is replaced by a violaceous discoloration of the skin. After five to seven days, the area of the bite progresses to aseptic necrosis, dry gangrenous slough and black eschar formation. An open ulcer forms as the eschar separates from viable tissue. Without treatment, the healing of this ulcer is very slow. Periods of up to four months were incurred in our series for the lesion to heal.² After the healing process is complete, a depressed scar of varying size remains at the site of the lesion. In a severe envenomization, a scarlatiniform rash may appear over the affected limb area of trunk. Systemic signs of toxicity including fever, chills, malaise, nausea, vomiting and arthralgia are frequently observed. The most serious effects of the brown recluse spider bite occur in children. Cases of massive intravascular hemolysis,⁶ convulsions,⁷ disseminated intravascular coagulopathy,⁸ and death,⁹ have been reported in the literature. The often mistaken diagnosis associated with the spider bite has been cellulitis or an abscess with the thought that streptococci were present.

The *L. reclusa* has been found mainly in the fifteen central states. Most cases have been reported from Arkansas, Kansas, Missouri, and Oklahoma. The brown recluse spider should be included in the differential diagnosis of a spider bite in South Carolina. Rare cases and specimens of the spider have been noted in New Jersey, Florida, Pennsylvania, North Carolina, and California. The brown recluse spider has been termed to be potentially more dangerous than the black widow spider because the natural habitat of the brown recluse spider is indoors. The spider is frequently found in closets, stored clothing, basements, and other similar quiet places. Most bites occurred at night in our series.² The spider is a nocturnal hunter and leaves its irregular web only at night in search of food. The recluse spider is not aggressive, and reports relate that it will only attack or bite if it is endangered or threatened.

The *L. reclusa* spider is slightly smaller than the black widow. The body is of medium size (10-15 mm. in length) with the females being slightly larger than the male. The spider may



Fig. 1. Example of the brown recluse spider with the dark band shaped like a violin which extends from the eyes to the end of the cephalothorax.

vary in color from yellow to dark brown. The carapace is flattened with six eyes (most spiders have eight) arranged in a curved row on the anterior portion of the cephalothorax. There are four legs on each side of the cephalothorax and the body is covered with microscopic hairs. Its legspan is about the size of a half-dollar. The spider is best identified by the dark band; shaped like a violin which extends dorsally from the eyes to the end of the cephalothorax. This marking is said to be species specific (Figure 1).

The venom from the brown recluse spider is complex, and nine protein components have been identified. The toxic components appear to have a molecular weight of approximately 24,000. The mechanism of action of the cytotoxic components of the venom is not fully understood. Circulating antibodies have not been found in humans bitten by the spider. Currently no antivenom has been produced by experimental studies for clinical use.

An *in vitro* test has been developed for detection of the brown recluse spider bite.¹⁰ Lymphocytes from patients believed to have been bitten are exposed to 50 mg. of venom protein *in vitro* with radioactive thymidine. If the patient has been bitten, then the lymphocytes will change to a blast form and take up the thymidine. It appears from recent reports, that the lymphocyte transformation test will turn positive approximately four to six weeks after the patient is bitten. The test is usually negative at the time of the spider bite. The lymphocyte transformation test recognizes those

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who are at risk and confirms mild and unusual manifestations of envenomization. Results from studies using this test indicate that many bites are mild, and they resolve spontaneously and leave no scar. Berger in his study¹¹ revealed a greater rate of lymphocyte transformation found in patients with mild clinical reactions to the spider bite. In contrast, those severe cases with only minimal lymphocyte transformation had the most severe reactions. His correlations^{10, 12} established that steroid therapy was generally not advantageous for treatment of the systemic reactions. Local antibiotic therapy was most effective for control of the local response. High dose steroids appear to have the disadvantage of diminishing the immune response to the acute bite and, also, subsequent bites. This was documented by experiments in which high dose steroids inhibited antigen processing and slowed the establishment of immune responsiveness. Berger documented two cases¹⁰ in which there were histories of multiple spider bites. Each subsequent bite was milder than the previous one. This suggested that the immune response was important in minimizing reactions in humans. Fardon¹³ in animal experiments showed that steroids, antihistamines, low molecular weight dextran and phenotolamine were of no value in the treatment of cutaneous loxoscelism. They reported that early total excision and split thickness skin grafting offered the only successful treatment to prevent the massive necrosis seen clinically. In a clinical study, Auer and Hershey⁵ suggested the early excision of any lesion over two cm. in diameter as the best treatment. Though the use of steroids currently is controversial, we suggest that the therapy administered to the patient with a recluse spider bite should de-

pend upon the clinical appearance of the reaction generated by the spider bite. The classification of spider bites as given by Auer and Hershey⁵ should be adhered to in general for grading the type of bite reaction. In our own experience, the mild reaction should be treated with local supportive therapy which includes antibiotics, tetanus prophylaxis and pain relief medication; the more severe bite should be treated with excision and a skin graft. Though we have used steroids for treating those bites which have fallen into the middle area of reactions with two to three centimeters of necrosis, these lesions have required the longest time to heal. From the studies mentioned and our own experience, definitive therapy for necrotic arachnidism in man is currently not adequate and requires further experimental investigation. A rapid test is currently needed for the family physician or emergency room physician for use when a patient is examined with a necrotic lesion originating in the geographical area the brown recluse spider is known to inhabit. The lymphocyte transformation test is generally unattainable due to the inavailability of the recluse spider venom. The venom has been difficult to obtain even for investigative use in our own lab. Considering the advances made during the past 15 years in recognition, pathophysiology and toxicology concerning loxoscelism, we forecast important medical progress within the next five years. Some advances should include (1) a better specific early treatment, (2) an easy available test for diagnosis, (3) possible immunization or an antivenom and (4) use of the specific cytotoxic properties of recluse venom for research in areas such as immunology and chemotherapy. □

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THE RIGHT TO REFUSE TREATMENT: EXPANDING FRONTIERS OF CIVIL LIABILITY FOR PHYSICIANS

WARNING! Read Package Insert

A lead editorial was intended to underscore this warning, but for reasons explained on the editorial page, this was not done. So suffice it to say: Antidysthanasia contracts have no legal status in South Carolina! Do not enter into any such agreement with your patient and expect it to offer you any protection. It will not!

Editor

ROBERT J. PARMLEY, J.D.*

The constitutional development of the right to refuse treatment has had a very painful birth as a legal concept because of the tremendous responsibility of decision making when a life hangs in balance. Since the Supreme Court of the United States has not directly ruled on the right to refuse treatment, the criteria used by the lower courts in deciding these cases varies from one jurisdiction to another.

One of the strongest proponents of the right to refuse treatment, or the right of self-determination as it is sometimes called, is Chief Justice Burger. In the *Application of the President and Directors of Georgetown College*, 331 F.2d. 1000, 331 F.2d. 1010 (App. D.C. 1964) Chief Justice Burger, then sitting as a circuit judge, strongly dissented to the ruling of the circuit court affirming an order that transfusions be given to a protesting twenty-five year old female Jehovah's Witness who was the mother of a seven-month-old child. Chief Justice Burger, after noting the fact that a waiver of liability had been signed by the patient, cited Justice Brandeis in *Olmstead v. United States*, 227 U.S. 438 (1928) where Justice Brandeis was the first to acknowledge the idea of a constitutional right of privacy by saying: "The makers of our Constitution... sought to protect Americans in their beliefs, their thoughts, their emotions and their sensations. They conferred, as against the Government, the right to be let alone—the most comprehensive of rights and the right most valued by civilized man."¹ Remarking about this statement, Chief Justice Burger said:

"Nothing in this utterance suggests that Justice Brandeis thought an individual possessed these rights only as to *sensible* beliefs, *valid* thoughts, *reasonable* emotions, or *well-founded* sensations. I suggest he intended to include a great many foolish, unreasonable and even absurd ideas which do not conform, such as refusing medical treatment even at great risk,"² (emphasis original). Many legal scholars have interpreted this statement as intimating a right to self-determination regardless of one's religious beliefs.³ Prior to this time it was thought that the right to refuse treatment was closely interrelated to the First Amendment's religious freedom clause rather than the Ninth Amendment's right to be let alone.

The test applied by most courts today concerning the right to refuse treatment is twofold: 1) has the patient validly and knowingly chosen that course for his life, and 2) is there a compelling state interest which justifies overriding that decision? Also, it has become an accepted practice in most jurisdictions that the judge make a personal visit to the patient to assess his competence.⁴ Whether or not a waiver of liability has been signed and whether there is a possibility that the patient's children may become wards of the state are some of the additional balancing factors in deciding if there should be state intervention.

Before looking at the civil liability of a physician in a right to refuse treatment case, it may be helpful for the reader to examine the differences between euthanasia, antidysthanasia and the right to refuse treatment. One factor distinguishing euthanasia from the right to refuse treatment is that by euthanasia

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one dies as a result of what is known in tort law as misfeasance, or an act of commission, which terminates the life process as opposed to the right to refuse treatment where there is nonfeasance, or omission of an act, which results in letting the body take its natural course towards death. The right to refuse treatment differs slightly from antidysthanasia, a Greek word meaning "failure to take positive action to prolong life."⁵ Antidysthanasia is a broad term which encompasses the right to refuse treatment. The difference between the two terms is that under the right to refuse treatment the decision is solely in the hands of the patient who is asserting the right (e.g., a terminally ill patient), whereas, antidysthanasia is not a right at all but rather a course of conduct which may be decided by the physician, patient, parent or guardian.

In considering civil liability for a physician or hospital it must be remembered that the basis of a doctor-patient relationship is informed consent. The fundamental premise of the doctrine of informed consent is that the physician's judgment is subservient to the patient's right to self-determination.⁶ Civil liability for battery will be imposed on a physician in a non-emergency situation if he treats a patient without the patient's consent. The physician will be found liable for damages even though he has the patient's consent if the physician renders treatment that is different from or more extensive than that authorized by the patient. Because the success of a battery action depends merely on the showing of an unauthorized touching or treatment, it is no defense for a physician to assert that the unauthorized treatment he gave the patient was done in a manner of professional competence or that it actually benefited the patient.⁷

It should be remembered, however, that in an emergency situation the law will imply the consent of the patient and thus create an implied contract between the doctor and patient. This implied contract will impose upon the physician a legal duty to use professional competence and care customary in similar professional communities among physicians engaged in his field of practice with the assumption that the patient wants to live.⁸ From the patient's point of view, an implied contract imposes on him an obligation to pay the reason-

able hospital and physician fees for the services that he was rendered.

Heretofore, a physician's liability to a patient usually fell into one of two categories: 1) a battery action resulting from the unauthorized treatment by the physician of the patient, and 2) a malpractice suit caused by the failure of a physician to use professional competence and the care customary in his professional community. With the development of the right to refuse treatment another type of liability will soon confront physicians, and at the same time, relieve many terminally ill patients from the uncertainty of the future. This liability will be based on contract law and will center around an antidysthanasia contract.

An antidysthanasia contract, unlike most contracts, states what a physician shall not be given consent to do. It is an enforceable contract that defines the scope of the physician's duty to the patient. If a competent patient stipulates in his contract with a physician that certain types of medical treatment are not to be taken, then the physician cannot render that treatment free from civil liability. If a physician, on the basis of moral conviction, breaches such a contract then he will be liable for the foreseeable damages of the breach such as room charge, medication, doctor's fees as well as any other expenses incurred by the patient after the time in which he or she would have died had it not been for the moral overreaching of the physician.⁹ The amount of recovery for the breach of the antidysthanasia contract may include a substantial amount of money, consequently, it provides an incentive on the part of physicians not to breach the contract but rather to respect the desires of the terminally ill patient. Prior to the creation of an antidysthanasia contract a terminally ill patient was denied the right of self-determination because the only legal tool the patient had was a "living will" which could either be respected or disregarded by the physician without fear of civil liability.

If an antidysthanasia contract should be breached, then the terminally ill patient or his family could assert the breach of contract as a defense to the payment of the physician and hospital fees.¹⁰ It is because of this contractual relationship that an antidysthanasia contract is such a useful and an effective tool for a

competent person who does not want certain types of treatment that may lead to an artificial prolongation of life and the possible financial depletion of his or her family's resources. The types of treatment not desired by the patient must be specifically stated in the contract. General terms like the "artificial prolongation of life" will remain in the physician's discretion unless otherwise narrowed by the contract.

The physician will not be found liable for his nonfeasance, or omission, where he has no legal duty to take positive action.¹¹ A real dilemma is created for the physician when a patient who has signed an antidysthanasia contract becomes unconscious in an emergency situation. What happens to the legal duty that the law would normally imply during an emergency? Is the physician's only choice in this situation to choose whether or not he wants to be sued for a breach of contract or for negligent malpractice? The answer to this question has not yet been resolved since antidysthanasia contracts have not yet been tested in the courts. However, a strong argument may be made in favor of the antidysthanasia contract dissolving the implied consent and legal duty imposed on a physician in a situation where a competent patient has signed the antidysthanasia contract just prior to a specific operation. Under this line of reasoning, it would be argued that the implied consent which creates a legal duty is only a legal fiction since the patient has previously clearly indicated that such consent was not to be given. The thrust of this argument is that implied consent is a rebuttable presumption that can be successfully rebutted by an antidysthanasia contract.

The antidysthanasia contract becomes of questionable validity when it is not signed by a competent patient just prior to a specific operation. If the contract is an open contract, without reference to a specific operation, then the later incompetency of a patient or his delirious behavior will most likely impose an implied contract and a legal duty on the physician, with the assumption that the patient wants to live, to use professional competence and care customary in similar professional communities among physicians engaged in his field of practice.

An antidysthanasia contract cannot impose

an enforceable duty on a physician to take an affirmative act to terminate the patient's life. This would constitute euthanasia and as such would be against public policy and unenforceable. An antidysthanasia contract will not be against public policy so long as the physician's role is one of non-feasance, or omission, as opposed to misfeasance, or commission.

If a physician is confronted by a patient who refuses treatment then he should first ascertain if the patient is mentally competent to refuse treatment. If the patient is competent then the physician should put a waiver of liability clause in the contract and have at least three witnesses sign the contract who could testify to the patient's competency upon entering the contract. However, even this does not give a physician full protection from civil liability because the issue of competency may be raised at a later trial. The safest way a physician may achieve full immunity is to get a court order and thereby fall under the shield of judicial immunity.

It would be unrealistic for physicians in South Carolina to dismiss the importance of an antidysthanasia contract simply because they have never seen nor heard of one. The antidysthanasia contract is an outgrowth of the right to refuse treatment, as well as a legal response to the unenforceability of a "living will." The popularity of the antidysthanasia contract is that the terminally ill patient who is the signatory of one possibly gets the "best of both worlds." If the contract is breached then the patient's family is free from the economic burden of a prolonged terminal illness. And, if the contract is enforced, then the patient's suffering, anxiety and bodily deterioration will cease when the dying process no longer has to compete with the "new biology" of the twentieth century.

Proposals

Because of the increasing number of malpractice suits, the doctor-patient relationship concerning the right to refuse treatment and antidysthanasia contracts should be clarified by statutory and judicial changes. This would benefit both the physician in his practice of medicine and the patient in his assertion of the right of self-determination. Since a physician is free to choose whether or not he will enter

RIGHT TO REFUSE TREATMENT

into an antidysthanasia contract with a patient, many physicians will probably shy away from the possible risk of incurring further liability under the present confused state of the law. This "chilling effect" of a patient's right of self-determination is intolerable when one considers the magnitude of the patient's decision and the alternatives open to him or her should this right be denied. A clarification of this area of the law would be in the best interests of the people of South Carolina.

One of the first statutory recommendations would be that the question of competency of a patient upon entering an antidysthanasia contract should be statutorily determinative as of the signing of three witnesses (excluding the physician). After this point in time, the question of competency should not be challenged anymore than the question of competency of a testator is challenged after three witnesses have signed his will.

A second statutory change should be that physicians and hospitals are granted civil and criminal immunity for nonfeasance when it is in conjunction with the performance of an antidysthanasia contract. The implied consent of a patient imposing a legal duty on the physician should be a rebuttable presumption which may be successfully rebutted by an antidysthanasia contract. This would relieve the physician of a potential legal dilemma he might find himself

in when a patient asserts his or her right to refuse treatment. Also, this would insure the patient the right of self-determination and the opportunity to decide for himself what death with dignity is. An immunity similar to this has already been granted to physicians when dealing with organ donors.¹²

A third proposal is that hospitals establish special ombudsmen-type boards as is done in some hospitals concerning abortion. The purpose of these boards would be to review antidysthanasia contracts to make sure they are specific enough and to aid the doctor in any discretionary power he has under the antidysthanasia contract, such as, whether a life is being artificially prolonged.¹³

A fourth and final proposal would be a judicial extension of post mortem arrangements of a dying person. This extension would permit the testator to make testamentary arrangements with his physician concerning antidysthanasia in the same manner that the current law allows for property disposition, burial provisions and authorization for organ transplants.¹⁴ The advantage of this would be that when a person has a sudden illness or accident which incapacitates him, his desires would be honored even though he failed to make a specific antidysthanasia contract with the hospital and physicians. □

WARNING! Read Package Insert

Antidysthanasia contracts have no legal status in South Carolina. They offer you no protection at all.
Editor

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President's Pages



Dear Fellow Physicians,

Your President would like to take this opportunity to commend the House of Delegates for their diligent work and their consideration of all the items of business before them at the meeting in Greenville on November 14 and 15. The medical profession of the State of South Carolina owes them a debt of gratitude.

In reviewing some of the major changes that have taken place in the State Association during the past several months, and in reviewing some of the proposed changes which are to be decided in the future, a definite trend of major importance can be seen.

There is a definite trend on the part of the State and Federal Governmental agencies and on the part of Health Insurance Carriers to place more and more decision-making authority in the hands of the medical profession regarding questions which affect both health care delivery and the professional activities of individual physicians.

Some of these items which demonstrate this trend are as follows:

1. The creation of the Joint Underwriters Association at the request of the SCMA.
2. The decision on the part of the Department of Health, Education and Welfare to select the Medical Care Foundation to implement PSRO in the State.
3. The agreement with Blue Cross - Blue Shield establishing the Peer Review Contract which will give the South Carolina Medical Association Committee final authority over disputed claims which Blue Cross - Blue Shield refers to the Committee.
4. The signing of the McLeod Bill by the Governor at the request of the South Carolina Medical Association, and the passage of a law postponing its implementation for one year, also at the request of the South Carolina Medical Association.

Also, with the House of Delegates accepting the resolution regarding reimbursement schedules for Medi-Care and Medi-Caid, we believe the intermediaries and Government agencies will work with the South Carolina Medical Association in an effort to create an implementation schedule which is more equitable for physicians than the present one.

5. The designation of the South Carolina Medical Association Committee on Continuing Education as the single certifying agency in the State for all post-graduate education programs seeking AMA certification.
6. The Medical Disciplinary Act: A new Act before the House of Delegates on November 15 was passed unanimously and was endorsed by the State Board of Medical Examiners; we believe we shall receive favorable treatment from the Board of Medical Examiners, the Attorney General, and that we will be able to get it accepted by the State Legislature.

We believe the willingness on the part of these groups to turn final authority in these matters over to the profession gives us a chance to prove that the profession can discipline itself, can negotiate reasonable fees that are not exorbitant, and can solve many of its own problems.

With the House of Delegates at the Convention on November 15 adopting the \$60.00 dues assessment for 3 more years, the South Carolina Medical Association Building is on sound financial footing. Prospects are good that vacant space will be rented in the next several months. As the activities and services of your Medical Association increase in the next several years, more and more space in this building will be occupied and used by your Association. I would like to express my personal gratitude, and the gratitude of your Council and Officers, for the House of Delegates unanimously passing this dues assessment for 3 more years.

As this is being written, your Delegates and President are on their way to the AMA Convention in Honolulu, and you will be receiving reports on that Convention in a later issue.

May I extend to each of you, and to your families and loved ones, Christmas greetings and best wishes for a safe and happy holiday season.

Sincerely,
C. Tucker Weston, M.D.
President

Maybe the patient's self-diagnosis is right. He could have hay fever. But that bright red nasal mucosa, along with the thick discharge and excoriation around the nares, strongly suggests that the main problem is a cold. Hay fever or another form of allergic rhinitis may or may not be an underlying factor.

If a complete history and examination rule out allergic rhinitis, the long-term outlook will be a lot more favorable than his own "diagnosis" would have indicated.

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Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as lacking substantial evidence of effectiveness as a fixed combination. Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses, such as the common cold, seasonal allergies, sinusitis, rhinitis, conjunctivitis and otitis. In these cases it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions, thereby affording relief from nasal stuffiness and postnasal drip.

CONTRAINDICATIONS: Hypersensitivity to antihistamines of the same chemical class. Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age. Because of its drying and thickening effect on the lower

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WARNINGS: Use in children. In infants and children particularly, antihistamine in overdose may produce convulsion and death.

PRECAUTIONS: Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery, etc. Patients receiving antihista-

mine should be warned against possible additive effect with CNS depressants such as alcohol, hypnotics, sedative tranquilizers, etc.

ADVERSE REACTIONS: Adverse reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash, urticaria, leukopenia, agranulocytosis, and thrombocytopenia; drowsiness; fatigue; giddiness; dryness of the mucous membranes; tightness of the chest; thickening of bronchial secretions; urinary frequency and dysuria; palpitation; hypertension; headache; faintness; dizziness; tinnitus; incoordination; visual disturbances; mydriasis; CNS depression and (less often) stimulant effect; anorexia; nausea; vomiting; diarrhea; constipation; and epigastric distress.

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Indications: Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products, excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.

Ⓜ Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on written or oral prescription and may be refilled 5 times within 6 months, unless restricted by state law.

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Editorials

Death and Dying, and Living

This month things just seemed to line up. The Karen Anne Quinlan affair made headlines for several weeks. For those who don't recall, this is the neither-dead-nor-alive girl whose parents wanted to cease mechanical life-sustaining measures and went to court to obtain this. Then I read several books about death, euthanasia, funerals. Then my Sunday School had a series on the meaning of death, and finally, my favorite preacher gave a session on Christian death and funerals. But then something happened that broke my concentration. You probably do not realize how much concentration it takes to turn out one of these simple little pieces. But something interrupted my concentration this month. I had mother-in-law trouble. For the first time in my life I had serious mother-in-law trouble. She died. And I mourn her. I mourn her very much.

I would like to tell you a little bit about her life. I think you might be interested. And I think maybe there is a lesson in it.

My mother-in-law was born of Swedish immigrant parents on a farm in Minnesota, went to nursing school in Minneapolis, and worked in a hospital in Chicago during the Al Capone era. While in Chicago she met and married a boy from New Hampshire who was there in school. Returning to New England with him, she found the Yankee reception a bit cool, but found plenty to do taking care of the seven children they had in ten years. Then, with seven children under ten years of age, the father suddenly died. Those were the days before insurance agents and life insurance, before social security and aid to dependent children, etc. So what to do, in a tiny (but beautiful) New England town, a stranger in a strange

land, with nothing, *nothing* at all but seven little children to raise.

Luckily, there was a hospital in another town 22 miles away. Those were the days of 12-hour shifts, six days a week. So every day of every week, except on Sunday, she walked about a half mile to the local train station to meet the 5:30 p.m. train, rode 22 miles, walked from the station 2 miles to the hospital, worked 12 hours, walked 2 miles, rode 22 miles, walked a half mile home at about 10:30 a.m. Remember this is in the mountains of New England, where the wind whips and the temperatures hover at 20-30° below zero in the winter. She slept 2 or 3 hours after getting home but was *always* up and dressed when her children got home from school. She never complained, never grumbled, and then never did to her last day. Every one of her children, except the oldest daughter who quit nursing school to marry into the founding family of the town, finished college or nursing school and all have gone on to be very worthwhile family people.

That is her story. Now for the lesson. True, this strong, brave, and able mother was exceptional. But if food stamps had been available, if aid to dependent children was handed out, if charity had been abundant, even with the good mother, I am sure in my own mind that some of those seven children would not now be self-sufficient. They would have learned to live on handouts and would never have gotten off. So, as hard hard hard as that life must have been, because of the good mother, it was better than living off charity.

My mother-in-law died, and I mourn her very much. R.I.P. □

EEK

Correction for October Issue of the Journal

Re: Acute epiglottitis vs. organophosphate poisoning in infancy: A case report, J S Carolina Med. Assoc. 71:11, 309, 1975.

It should be noted that the name of the primary author of this article, Carroll S. Brown, M.D., was omitted from the original printing. Dr. Brown will appear in the Journal 1975 Index in reference to this page and the initial page of his article.



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The Division of Continuing Education of the Medical University of South Carolina will offer the Seventh Annual Family Practice Refresher Course from February 15-21, 1976. Forty (40) AAFP Credit Hours will be awarded for full-time attendance at this course. Lectures will be presented at the Mills Hyatt House Hotel with visits to various units of the Medical University complex for tours and demonstrations. Among the topics to be covered are internal medicine, pediatrics, surgery, psychiatry and community health. A featured guest speaker will be Nicholas J. Pisacano, M.D., Executive Director and Secretary of the American Board of Family Practice, who will present a lecture on the Family Practice Board Examinations. Optional workshops for additional credit hours will also be offered.

Registration is open now through February 1, 1976. Enrollment is limited to 75, and tuition is \$150.00 payable in advance on or before February 1, 1976. The Social Hour and Banquet on Wednesday evening is included in the tuition fee. Spouses are cordially invited. A block of rooms is being held at special convention rates at the Mills Hyatt House Hotel until January 25. To insure a room, please make your reservations before that date.

A registration desk will be open from 6:30-8:30 p.m., Sunday evening, February 15, in the Middleton Room on the first floor of the hotel for the convenience of those participants wishing to complete their registration at that time. Final registration will be in the pre-assembly area at 8:00 a.m., Monday, February 16.

Please detach and return

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Sponsor	Department of Neurology University of Miami School of Medicine
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Dates	February 2-6, 1976
Meeting Site	Hotel Fontainebleau Miami Beach, Florida
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For Information & Registration Information: Division of Continuing Medical Education
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Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdose; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdose may cause severe, even fatal, respiratory depression. Signs of overdose include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

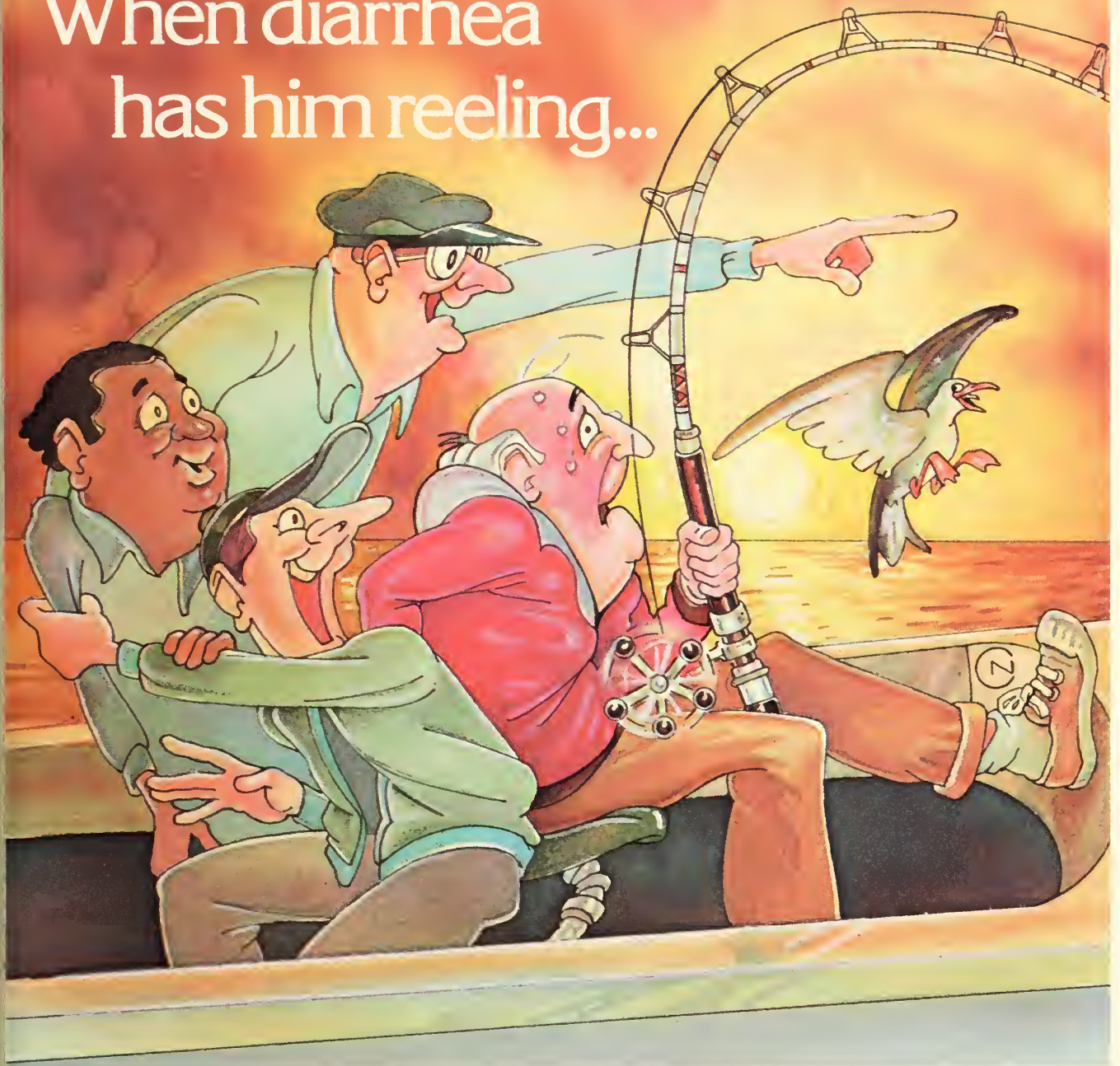
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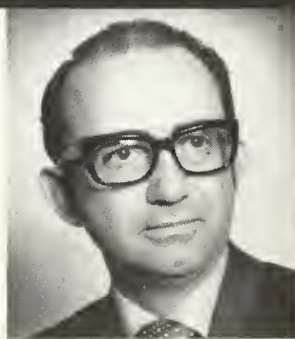
Each tablet and each 5 ml of liquid contain diphenoxylate hydrochloride 2.5 mg (Warning: May be habit forming); atropine sulfate 0.025 mg

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005





Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo*.
- Usual adult dosage for Antivert/25 for vertigo*: one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG 
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert[®]/25 (meclizine HCl) 25 mg. Tablets for vertigo*

Ivan Illich Faults World Health Care

Within the last decade the medical establishment has become a major threat to health and should be deprofessionalized to serve mankind to best advantage, says Dr. Ivan Illich.

His plea for a reversal in a worldwide trend toward declining health care and rising health services came during an *Encyclopaedia Britannica* endowed lecture at the University of Edinburgh in Scotland. The annual lectures have featured a world-renown figure since their inception in 1968 to celebrate the 200th anniversary of the encyclopaedia, which was first published in Edinburgh. The lecture will be published and distributed as a pamphlet.

Dr. Illich founded and directs the Centro Intercultural de Documentacio (CIDOC) in Cuernavaca, Mexico. It is an education center devoted to improving the cultural and social environment of the Latin American people but is viewed by some as a center for revolutionary activity. It was founded in 1961, growing out of Dr. Illich's experience as vice-chancellor of the Catholic University of Puerto Rico and as a priest assigned to a parish of Puerto Ricans in New York City, to which he had come fresh from his ordination in Rome.

Convinced that the church should not be identified with any kind of political activity, he requested, and was granted by his religious superiors, a suspension from his priestly functions.

"Only the organic damage done by the industrial production of food can rival the ill health induced by doctors," Illich said in this lecture.

He pointed out that during the past 20 years the life expectancy of adult male Americans has declined while health care costs have risen dramatically. The U.S. price index has increased by about 74 percent, he noted, while the cost of medical care has escalated by 330 percent.

At the same time, Illich continued, public expenditures for health care increased tenfold, out-of-pocket payments for health services rose threefold, and the cost of private insurance eighteenfold. "The cost of community hospitals has risen 500 percent since

1950," Illich stated. "The bill for patient care in major American hospitals rose even faster, tripling in eight years. Administrative expenses multiplied by a factor of seven, laboratory costs by a factor of five. Building a hospital bed now costs \$65,000, of which two-thirds goes towards mechanical equipment written off or made redundant within ten years or less."

Medicine in England can be similarly criticized, Illich said. While life expectancy in that country has not yet declined, the chronic diseases of middle-aged men have shown an increase, as they did a decade earlier in the U.S.

Citing figures for other nations, Illich pointed out that in the Soviet Union physician and hospital days per capita have tripled over the same period, and in China the medical-technological establishment has grown even faster. "The rate at which people become dependent on physicians appears to bear no relation to their form of government," Illich theorized.

"Medicine cannot do much for illness associated with aging. It cannot cure cardiovascular disease, most cancers, arthritis, multiple sclerosis, advanced cirrhosis, or the common cold.... Most professional intervention in their treatment not only heightens old people's pain — if successful, it also protracts it. One is therefore surprised to discover the extent to which resources are spent on the treatment of old age. While 10 percent of the U.S. population is above 65, 28 percent of health care expenditures are made on behalf of this minority. The old are outgrowing the remainder of the population at a rate of 3 percent, while the per capita cost of their care is rising at a rate of 6 percent. Gerontology takes over BNP. This misallocation of manpower, resources, and social concern will generate unspeakable pain as demands swell and resources dry up...."

Since the U.S.-Soviet agreement on scientific cooperation in the conquest of space, cancer, and heart disease, coronary care units have become symbols of peaceful progress and arguments for rising taxes, Illich said.

"They require three times the equipment and five times the staff needed for normal patient care; 12 percent of graduate nurses find jobs in such units. They also demonstrate

IVAN ILLICH FAULTS WORLD HEALTH CARE

the meaning of professionally approved embezzlement. Large-scale studies comparing results of patient care in these units with the home treatment of comparable patients have yet to demonstrate any advantage. The therapeutic value of heart-control stations is probably the same kind as that of space flights: seen on TV, they provide a rain dance for millions who learn to trust science and who cease to care for themselves."

Illich went on to say that "beyond a certain point, the production and delivery of medical care produces more ailments than it can heal. Social security guarantees painful survival more democratically and effectively than the most pitiless gods...."

"Medical interventions have not affected total mortality rates: at best they have shifted survival from one segment of the population to another. Dramatic changes in the nature of disease afflicting western societies during the last 100 years are well documented. First industrialization exacerbated infections, which then subsided. Tuberculosis peaked over a 50-75 year period and declined before either the tubercle bacillus had been discovered or anti-tuberculous programs had been initiated. It was replaced in Britain and the U.S. by major malnutrition syndromes — rickets and pellagra, which peaked and declined to be replaced by diseases of early childhood, which in turn gave way to duodenal ulcers in young men. When that declined the modern epidemics took their toll — coronary heart disease, hypertension, cancer, arthritis, diabetes, and mental disorders. At least in the U.S., death rates from hypertensive heart disease seem to be declining. Despite intensive research, no connection between these changes in disease patterns can be attributed to the professional practice of medicine...."

"Longevity owes much more to the railroad and to the synthesis of fertilizers and insecticides than it owes to new drugs and syringes." Illich went on to say. He pointed out that while professional practice is ineffective, it is increasingly sought out. "This technically unwarranted rise of medical prestige can only be explained as a magical ritual for the achievement of goals that are beyond technical and political reach. It can be countered only through legislation and political action that favor the deprofessionalization of health care."

"...Deprofessionalization does not mean the elimination of modern medicine, nor obstacles to the invention of new ones, nor necessarily the return to ancient programs, rituals, and devices. It means that no professional shall have the power to lavish on any one of his patients a package of curative resources larger than that which another person could claim on his own. Finally, the deprofessionalization of medicine does not mean disregard for the special needs which people manifest at special moments of their lives; when they are born, break a leg, marry, give birth, become crippled, or face death. It only means that people have a right to live in an environment that is hospitable to them at such high points of experience."

The level of public health corresponds to the degree to which the means and responsibility for coping with illness are distributed among the total population, Illich summarized. "That society which can reduce professional intervention to the minimum will provide the best conditions for health." □

Morris Village

Prototype for Treatment of Drug and Alcohol Addiction

Last month the S. C. Department of Mental Health officially opened the Earle E. Morris Jr. Alcohol and Drug Addiction Treatment Center, a facility already considered by mental health professionals to be a forerunner in the nation in the treatment of alcohol and drug addiction.

According to State Commissioner of Mental Health, Dr. William S. Hall, Morris Village, as the new \$3.3 million center is called, embodies several new approaches in the treatment of addiction. It employs the village concept, a treatment method in which addicts enter a residential community designed to meet all of their needs — emotional, physical, social and spiritual.

Life among the village's residential cottages, food centers, and recreation and therapy areas allows residents to progress along a continuous treatment plan in a comfortable setting. Every person with whom the residents come in contact is therapeutically helpful, from the doctors, nurses and social workers to maintenance personnel and other patients. In short, the village concept is a therapeutic community designed to free the patient of addiction while strengthening his self-will and resolve to remain free.

In addition, Hall said Morris Village incorporates the catchment area treatment design, which divides South Carolina into four equal areas in terms of population admitted to the village. Each geographic area is assigned an interdisciplinary team whose members are familiar with the resources, personnel and influences in that area.

Composed of a psychologist, social worker, vocational rehabilitation counselor, activity therapist, chaplain and nurse, the team from the patient's area sets up that patient's treatment program, monitors his progress and oversees his transition back into the community. The catchment treatment method is designed to reduce the patient's confusion, build his self-confidence and strengthen his ability to relate to his surroundings.

Dr. Hall also cited a third innovation at the

new center: its architecture. Morris Village is architecturally designed to provide what today's professionals consider the best environment for rehabilitating addicts. For example, most addicts have a sense of the world closing in on them. The residential cottages at Morris Village have high vaulted ceilings intended to counteract the addict's sense of claustrophobia. The cottages also contain a central living, eating, cooking and activity space planned to recreate a home-like atmosphere while providing the residents with their own semi-private rooms.

A fourth unusual trait of the new facility and its programs is the focus on the individual patient as opposed to his problem. Morris Village does not distinguish between alcoholics and drug addicts. It perceives its residents as persons with chemical abuse problems and seeks to treat the patient instead of his habit.

Village programs offer a wide range of interdisciplinary services for alcohol and drug addicts, whether male or female, teenager or adult. Over seventy percent of the center's admissions are voluntary. Many of these come from community agencies that have exhausted available local services and consider temporary removal from the community and entry into the center's intensive treatment regimen as the best alternative for the patient and his family.

When patients first arrive at the village, they spend up to a week in the detoxification unit working on a safe, comfortable withdrawal. At this point in their treatment, they are suffering from acute addiction symptoms: malnourishment, physical weakness and emotional disorientation.

From detoxification, they move into one of the residential cottages, where the stay averages six weeks. Here, residents are motivated to perform daily tasks and interact with their fellow residents. They are encouraged to participate in occupational and recreational therapy going on in other buildings at the village. They receive assistance in improving their family and other social relations.

MORRIS VILLAGE. DRUG AND ALCOHOL ADDICTION CENTER

After residents leave the village program, they keep in close contact through an extensive aftercare service maintained by the staff. This follow-up program, along with Alcoholics Anonymous, insures continuation of therapy at the community level and cuts down on the readmission rate.

Located seven miles north of Columbia, S.C. at 610 Faison Drive, Morris Village has been occupied since September 3 when patients and staff moved from their temporary quarters at nearby Crafts-Farrow State Hospital. Presently, there are 129 residents and 104 employees at the village. Full occupancy of the 186-bed facility is expected by Christmas, 1975, when construction will be complete.

The village complex itself is composed of 22 buildings located in a pine forest on the shores of a 70-acre man-made lake. A library, canteen, clothes cleaning facilities, vending machines, pay telephones, and daily newspaper stands are located on the village grounds.

Since it began as a pilot project in 1971 at Crafts-Farrow State Hospital, over 1700 South Carolinians have benefited from the services of the Alcohol and Drug Addiction Center.

While South Carolina's new addiction center represents the long-held dreams and hopes of many state mental health professionals and legislators, one man, more than any other, helped the center come into being. This is the man for whom the center is named, South Carolina's former lieutenant-governor, Earle E. Morris Jr.

From his influential position as chairman of the S. C. Legislative-Governor's Committee on Mental Health and Mental Retardation for 12 years, Morris is credited with laying the groundwork for the passage of many important pieces of mental health legislation, including the act which created the Addiction Treatment Center in 1968. He also directed the efforts to levy the special tax and funds which constructed the center.

When the S. C. Mental Health Commission, the governing board of the S. C. Department of Mental Health, decided to name the Addiction Center for Morris in March, 1975, Commission Chairman C. M. Tucker Jr. praised the legislator for his 24 years of service to the cause of mental health. Tucker called Morris "a key force behind the progress the Department has

made in the last decade — progress not only in providing South Carolinians with better staff, facilities and treatment programs but progress also in lessening the stigma associated with mental illness."

Tucker also commended the Pickens, S.C., native for backing the commission in its request for separate bonding authority for major construction projects in the department, a move which has allowed the department to expand its services even in times of economic stress. And Morris was cited for his role in sponsoring key pieces of community mental health legislation which helped the S. C. Department of Mental Health set the national trend toward community mental health programs.

In recognition of meritorious service to the cause of mental health, Republican Governor James B. Edwards appointed Morris, a Democrat, to the seven-member S. C. Mental Health Commission in June, 1975.

At the ribbon cutting after the Oct. 27 dedication of the new village, Morris allowed his young son, Earle E. Morris III, to cut the ceremonial ribbon as other members of the Morris family, dignitaries and department employees looked on. With this symbolic act, seven years of planning and hard work became a reality for the S. C. Department of Mental Health in its efforts to treat the illness known as chemical abuse. □

Medical University of South Carolina

COLLEGE OF PHARMACY / HOSPITAL DEPARTMENT OF PHARMACY

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Discreet formulations of four well regarded drugs for the relief of bronchial distress—Potassium Iodide, Glyceryl Guaiacolate, Aminophylline, Ephedrine with Phenobarbital (to lessen cardiac stimulation).



INDICATIONS: For the prompt symptomatic relief of bronchial asthma, emphysema and bronchiectasis. The Mudranes dilate the bronchi and liquefy mucus plugs. **DOSAGE:** Tablet; One tablet with a full glass of water 3 or 4 times daily as required. Divide tablet for child's dose, Elixir; Children, 1 cc for each 10 lbs. of body weight. May be repeated 3 or 4 times a day. Adult, one tablespoonful 4 times daily. All doses should be followed with a glass of water.

CONTRAINDICATIONS: Aminophylline/Theophylline is contraindicated in the presence of severe cardiac arrhythmias and patients with massive myocardial damage. Ephedrine, in presence of severe heart disease, extreme hypertension, and in hyperthyroidism. Phenobarbital, in porphyria and in patients with known phenobarbital sensitivity. Potassium Iodide, in pregnancy (to protect the fetus against possible iodine-induced depression of thyroid activity), in tuberculosis (produces gumma dissolution), and in acne; also in the presence of known iodide sensitivity. **PRECAUTIONS:** Aminophylline/Theophylline should be avoided in patients with massive myocardial damage and/or severe cardiac

arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdosage. Potassium Iodide: Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing anginal pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdosage. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

HOW SUPPLIED: Mudrane and Mudrane GG available in bottles of 100 and 1000 tablets; Mudrane-2 and Mudrane GG-2 in 100s; Elixir in pints and half-gallons.

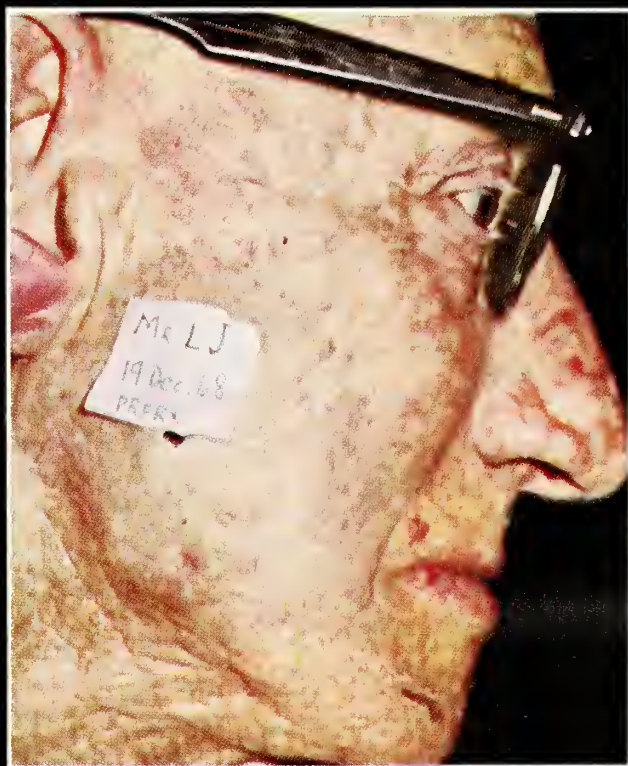
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the sun and solar keratosis...

Overexposed



and often underdiagnosed

Solar keratosis is not an uncommon medical problem.

Of course, the prevalence of keratotic lesions is greater in locations south of the 38th parallel—the so-called "Solar Keratosis Belt"—receiving the greatest amounts of solar radiation. However, solar keratosis can occur among any light-skinned population, usually in persons over 40, wherever people are subject to extended exposure to the sun.

Solar keratoses are generally not difficult to identify.

These skin lesions are usually multiple, flat or slightly elevated, brownish or red in color, papular, dry, rough, adherent and sharply defined. They are found on areas of the skin having extensive exposure to sunlight. Clinical characteristics of the lesions, their predominant location on exposed surfaces, the age of the patient and his skin type are important considerations in the diagnosis.

Solar keratoses can, and should, be treated because they are potentially premalignant.

Chronic exposure to sunlight frequently leads to degenerative changes in the skin. This can often result in the development of multiple, potentially premalignant keratotic lesions. Therefore, early detection and treatment is advisable.

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to

respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dis-

pensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris (hydroxymethyl) aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

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Roche Laboratories
Division of Hoffmann-La Roche Inc.
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Case history for patient photographed at left on file, Hoffmann-La Roche Inc., Nutley, New Jersey.

The South Carolina Medical and Dental Scholarship Fund

The South Carolina Medical and Dental Scholarship Fund was established by the General Assembly in 1974. Its purpose is to induce physicians and dentists to enter general practice in communities which are considerably short of doctors or dentists. The South Carolina Board of Health and Environmental Control administers the Fund with monies appropriated by the General Assembly.

The Board sets a designated time period each year in which it will receive and consider all applications for loans from students who have been legal residents of South Carolina for at least one year immediately preceding their application and who are acceptable for enrollment in any accredited medical school or dental school within the United States. The Board investigates the ability, character, financial needs, and qualifications of each applicant, and considers the intent of the applicant to practice medicine or dentistry in a predominantly rural area.

To the extent that funds are available, the Board may grant to each applicant deemed by the Board to be qualified a loan not exceeding \$6200 a year for not more than four years to defray tuition, living expenses, and other school related expenses. Each loan is based upon the condition that the applicant apply for a license to practice medicine or dentistry in South Carolina at the earliest practicable opportunity and that, within six months after the applicant is so licensed to practice, he will engage in the general practice of medicine or dentistry in a service area within this State which has a ratio of not more than one doctor for each 2000 people or a ratio of not more than one dentist for each 6000 people. The Board is required to approve a deferment of the required entry into practice during the time the applicant is engaged in internship or residency training in the field of general practice or family practice.

The Board prepares annually a list of medical service areas and dental service areas and the ratios of doctors and dentists to the population in each service area, using the popula-

tion figures of the latest official United States Census and the latest directories of the State Board of Medical Examiners and the State Board of Dentistry. All areas of the State are included in these service areas. Medical service areas have a minimum population of 2000 and dental service areas have a minimum population of 6000 and each such area has at least one town or municipality, whether or not incorporated, with a population of at least 500. The applicant may choose the service area in which he desires to practice.

Practice in a shortage area cancels the loan, year for year, and three years of practice will cancel a four-year loan. If the applicant cannot fulfill his obligation for justifiable cause, he may repay the loan with 7% interest. If he fails to practice in accordance with the terms of his contract without justifiable cause, three times the amount loaned plus 7% interest thereon is due and payable. □

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INDICATIONS: Therapeutically (as an adjunct to systemic therapy when indicated) for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyoderms (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing. **CONTRAINDICATIONS:** Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to



neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome Co.
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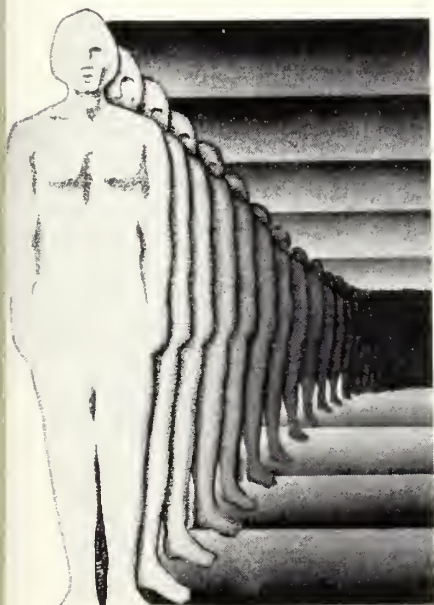
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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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Important Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents including the sulfonamides. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period. Contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.

Warnings: Safe use in pregnancy has not been established. Teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

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eral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

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